1

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FOR: Jan Delaval
OR
John Dunkleman

Scientific and Technical Information Center

SEARCH REQUEST FORM

Date: 3/27/00 Requester's Full Name: BENNETT CECCA Examiner #: 73815

Art Unit: 1627 Phone (305) 7776 Serial Number: 09/011,940

Results Format Preferred (circle) (PAPER) DISK E-MAIL

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: see ATTACHED

Inventors (please provide full names): "

Earliest Priority Date: 8/2/95

Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known.

For Sequence Searches Only *Please include all pertinent information (parent, grandchild, divisional, or issued patent numbers) along with the appropriate serial number.*

elected invention : claims 1-2, 17-25, 32-50 [method]

elected species : Glucose + GLP-1 (Glucagon-like peptide 1)
- see addition species of claim 22

Please

1. search clms 1-2, 17-25 & 32-50 in relevant databases
2. search elected embodiment
   Glucose + GLP-1
   * also search peptide species of clm 22
3. search inventors
4. can combine 3+ 1&2

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MAR 27 2000
TECH/CHEM DIVISION
(STIC)

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Searcher: Jan

Searcher Phone #: 4498

Searcher Location: _____

Date Searcher Picked Up: 4/00

Date Completed: 4/10

Searcher Prep & Review Time: 15

Online Time: 90

Type of Search

_____ NA Sequence (#)
_____ AA Sequence (#)
_____ Structure (#)
✓ Bibliographic
_____ Litigation
_____ Fulltext
_____ Other

Vendors and Cost

✓ STN
_____ Dialog
_____ Questel/Orbit
_____ Dr.Link
_____ Lexis/Nexis
_____ Westlaw
_____ WWW/Internet
_____ In-house sequence systems (list)
_____ Other (specify)

=> fil reg

FILE 'REGISTRY' ENTERED AT 13:10:59 ON 10 APR 2000
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STRUCTURE FILE UPDATES: 9 APR 2000 HIGHEST RN 261502-99-2
DICTIONARY FILE UPDATES: 9 APR 2000 HIGHEST RN 261502-99-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 11, 2000

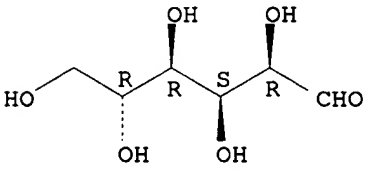
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d ide can 19

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN **58367-01-4** REGISTRY
CN DL-Glucose (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-Glucose
CN dl-Glucose
CN Glucose
FS STEREOSEARCH
DR 111688-73-4
MF C6 H12 O6
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CEN, CIN, IMSDIRECTORY, MEDLINE, PIRA, PROMT, TOXLIT, TULSA, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



83 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
83 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:167313

REFERENCE 2: 132:87465

REFERENCE 3: 132:47466

REFERENCE 4: 132:8597

REFERENCE 5: 132:3529

REFERENCE 6: 131:287966

REFERENCE 7: 131:269262

REFERENCE 8: 131:235507

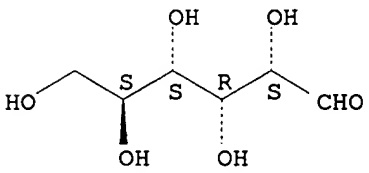
REFERENCE 9: 131:99030

REFERENCE 10: 131:60251

=> d ide can l11

L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN **921-60-8** REGISTRY
CN L-Glucose (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN L(-)-Glucose
CN l-Glucose
FS STEREOSEARCH
MF C6 H12 O6
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, GMELIN*, IPA, MSDS-OHS, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



670 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
672 REFERENCES IN FILE CAPLUS (1967 TO DATE)
8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 132:189684

REFERENCE 2: 132:178509

REFERENCE 3: 132:152031

REFERENCE 4: 132:146911

REFERENCE 5: 132:117733

REFERENCE 6: 132:85166

REFERENCE 7: 132:26663

REFERENCE 8: 131:349198

REFERENCE 9: 131:303302

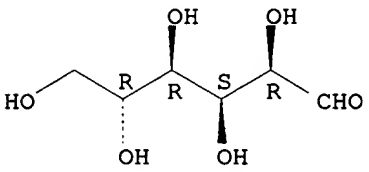
REFERENCE 10: 131:297740

=> d ide can l13

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN **50-99-7** REGISTRY
CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:
CN (+)-Glucose
CN Anhydrous dextrose
CN Cartose
CN Cerelose
CN Cerelose 2001
CN Corn sugar
CN D(+)-Glucose
CN Dextropur
CN Dextrose
CN Dextrosol
CN Glucolin
CN Glucose
CN Glucosteril
CN Grape sugar
CN Staleydex 111
CN Staleydex 333
CN Sugar, grape
CN Tabfine 097(HS)
CN Vadex
FS STEREOSEARCH
DR 8012-24-6, 8030-23-7, 162222-91-5, 165659-51-8, 50933-92-1, 80206-31-1
MF C6 H12 O6
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIPPR*, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TULSA, ULIDAT, USAN, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



105097 REFERENCES IN FILE CA (1967 TO DATE)
1743 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
105196 REFERENCES IN FILE CAPLUS (1967 TO DATE)
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 132:216291

REFERENCE 2: 132:216285

REFERENCE 3: 132:216070

REFERENCE 4: 132:213079

REFERENCE 5: 132:212732

REFERENCE 6: 132:212726

REFERENCE 7: 132:212596

REFERENCE 8: 132:212500

REFERENCE 9: 132:211567

REFERENCE 10: 132:209522

=> d ide can l19

L19 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN **59392-49-3** REGISTRY
CN Gastric inhibitory polypeptide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Gastric inhibitory peptide
CN GIP
CN Glucose-dependent insulinotropic peptide
CN Glucose-dependent insulinotropic polypeptide
MF Unspecified
CI PMS, MAN
PCT Manual registration
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, NAPRALERT, TOXLINE, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
957 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
959 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:193674

REFERENCE 2: 132:150280

REFERENCE 3: 132:150142

REFERENCE 4: 132:117676

REFERENCE 5: 132:103130

REFERENCE 6: 132:59445

REFERENCE 7: 132:45230

REFERENCE 8: 132:31744

REFERENCE 9: 132:31743

REFERENCE 10: 132:9115

=> d ide can l21

L21 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN **89750-14-1** REGISTRY
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glucagon-related peptide I
OTHER NAMES:
CN Glucagon-related peptide 1
CN PN: WO9947161 SEQID: 1 claimed sequence
CN PN: WO9947161 SEQID: 7 claimed sequence
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, EMBASE, IPA, MEDLINE, TOXLINE, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
529 REFERENCES IN FILE CA (1967 TO DATE)
29 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
531 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:212699

REFERENCE 2: 132:176061

REFERENCE 3: 132:176059

REFERENCE 4: 132:175839

REFERENCE 5: 132:161338

REFERENCE 6: 132:147179

REFERENCE 7: 132:146904

REFERENCE 8: 132:146715

REFERENCE 9: 132:132452

REFERENCE 10: 132:132385

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 13:11:43 ON 10 APR 2000
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FILE COVERS 1967 - 10 Apr 2000 VOL 132 ISS 16
FILE LAST UPDATED: 9 Apr 2000 (20000409/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Now you can extend your author, patent assignee, patent information, and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.

=> d his

(FILE 'HCAPLUS' ENTERED AT 12:54:41 ON 10 APR 2000)
DEL HIS
E NAUCK M/AU
L1 52 S E3,E4,E11,E12
E WAGNER F/AU
L2 374 S E3
E WAGNER FRED/AU
L3 67 S E3,E7,E9,E10,E15,E18,E20,E23
E BIONEB/PA,CS

```
L4           24 S E5-E14
L5          514 S L1-L4
L6            1 S L5 AND PARENTERAL?
L7            0 S L1 AND L2,L3
L8            3 S L1-L3 AND L4

     FILE 'HCAPLUS' ENTERED AT 12:57:48 ON 10 APR 2000
                S 50-99-7/REG# OR  921-60-8/REG# OR  58367-01-4/REG#

     FILE 'REGISTRY' ENTERED AT 12:58:19 ON 10 APR 2000
L9            1 S 58367-01-4/RN

     FILE 'HCAPLUS' ENTERED AT 12:58:20 ON 10 APR 2000
L10          83 S L9

     FILE 'REGISTRY' ENTERED AT 12:58:22 ON 10 APR 2000
L11           1 S 921-60-8/RN

     FILE 'HCAPLUS' ENTERED AT 12:58:22 ON 10 APR 2000
L12         677 S L11

     FILE 'REGISTRY' ENTERED AT 12:58:24 ON 10 APR 2000
L13           1 S 50-99-7/RN

     FILE 'HCAPLUS' ENTERED AT 12:58:25 ON 10 APR 2000
L14      105723 S L13
L15      106038 S L14 OR L12 OR L10
L16          20 S L5 AND L15
L17          48 S L5 AND GLUCOSE
L18          49 S L16,L17

     FILE 'REGISTRY' ENTERED AT 12:59:03 ON 10 APR 2000

     FILE 'REGISTRY' ENTERED AT 12:59:09 ON 10 APR 2000
L19           1 S 59392-49-3

     FILE 'HCAPLUS' ENTERED AT 13:00:12 ON 10 APR 2000
L20        1432 S L19 OR GIP OR GASTRIC()INHIBIT?()(POLYPEPTIDE OR PEPTIDE) OR

     FILE 'REGISTRY' ENTERED AT 13:00:22 ON 10 APR 2000
L21           1 S 89750-14-1

     FILE 'HCAPLUS' ENTERED AT 13:01:30 ON 10 APR 2000
L22         958 S L21 OR GLUCAGON()(LIKE OR RELATED)()PEPTIDE()(1 OR I)
L23        1118 S L22 OR GLP()(1 OR I)
L24          30 S L5 AND L23
L25          22 S L18 AND L24
L26          15 S L25 AND 7 36
L27          15 S L25 AND 7 36 AMIDE
L28          15 S L26,L27
L29           1 S L28 AND COMPOSITION
L30        1146 S L23 OR GLUCAGONLIKE()(PEPTIDE OR POLYPEPTIDE)
L31          30 S L5 AND L30
L32          22 S L31 AND L18
L33          15 S L32 AND 7 36 AMIDE
L34           1 S L33 AND   COMPOSITION
L35           1 S L34 AND GASTRIC INHIBIT? PEPTIDE
L36           2 S L32 AND FEED?
L37           3 S L32 AND FOOD?
L38           3 S L32 AND NUTRI?
L39           6 S L36-L38
L40           1 S L39 AND 63/SC,SX
L41           5 S L39 NOT L40
L42           5 S L41 AND L30
L43          21 S L32 NOT L40
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FILE 'REGISTRY' ENTERED AT 13:10:59 ON 10 APR 2000

FILE 'HCAPLUS' ENTERED AT 13:11:43 ON 10 APR 2000

=> d all 140

L40 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:192193 HCAPLUS
DN 126:190958
TI Composition and medium for parenteral **nutrition**
IN **Nauck, Michael**
PA Nauck, Michael, Germany
SO Ger. Offen., 3 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM A23L001-29
ICS A23L001-305; A61K038-22
CC **63-6** (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19530865	A1	19970227	DE 1995-19530865	19950822
	WO 9707814	A1	19970306	WO 1996-US13615	19960822
	W: AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT				
	CA 2227278	AA	19970306	CA 1996-2227278	19960822
	AU 9669006	A1	19970319	AU 1996-69006	19960822
	EP 851763	A1	19980708	EP 1996-929722	19960822
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1195992	A	19981014	CN 1996-196938	19960822
	JP 11514972	T2	19991221	JP 1996-510445	19960822
PRAI	DE 1995-19530865		19950822		
	WO 1996-US13615		19960822		

AB The compn. contains **glucagonlike peptide** 1 (7-36-amide) and/or gastric inhibitory peptide, preferably in a pharmaceutical form for parenteral **feeding**.
ST parenteral pharmaceutical glucagonlike gastric inhibitory peptide
IT **Nutrients**
Parenteral **feeding**
Parenteral solutions (drug delivery systems)
(compn. and medium for parenteral **nutrition**)
IT Amino acids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compn. and medium for parenteral **nutrition**)
IT **50-99-7**, **Glucose**, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compn. and medium for parenteral **nutrition**)
IT 59392-49-3, Gastric inhibitory polypeptide **89750-14-1**, **Glucagon-related peptide I**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compn. and medium for parenteral **nutrition**)

=> d 143 bib abs hitrn tot

L43 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:795694 HCAPLUS
DN 132:31283
TI **Glucagon-like peptide-1** improves .beta.-cell response to **glucose** in subjects with impaired **glucose** tolerance
IN Goke, Burkhard; Byrne, Maria
PA **BioNebraska, Inc., USA**
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964061	A1	19991216	WO 1999-US10040	19990507

PI
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-89044 19980612
AB A compn. for the treatment of impaired **glucose** tolerance (IGT) including a compd. which binds to a receptor for **glucagon-like peptide-1**, and a pharmaceutical carrier. The amt. of the compd. present is an effective amt. to improve pancreatic .beta.-cell sensitivity to blood **glucose** levels in a human with IGT. Also, a method for improving the pattern of insulin secretory responses in a human with IGT by administering to the human a compn. comprising a compd. which binds to a receptor for **glucagon-like peptide-1** and a pharmaceutical carrier.
IT **50-99-7**, D-**Glucose**, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**glucagon-like peptide-1** or a compd. that binds to the **GLP-1** receptor improves .beta.-cell response to **glucose** in subjects with impaired **glucose** tolerance)
IT **89750-14-1**, **Glucagon-like peptide I 89750-14-1D**, **Glucagon-like peptide I**, variants
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glucagon-like peptide-1** or a compd. that binds to the **GLP-1** receptor improves .beta.-cell response to **glucose** in subjects with impaired **glucose** tolerance)

L43 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:719697 HCAPLUS
DN 129:310971
TI **Glucagon-like peptide 1** (**GLP-1**). A potent gut hormone with a possible therapeutic perspective
AU **Nauck, M. A.**
CS Department Medicine, Knappschafts-Krankenhaus, Ruhr-University, Bochum, D-44892, Germany
SO Acta Diabetol. (1998), 35(3), 117-129
CODEN: ACDAEZ; ISSN: 0940-5429
PB Springer-Verlag
DT Journal; General Review
LA English

AB A review with 166 refs. **Glucagon-like peptide 1** (**GLP-1**) is a physiol. incretin hormone from the lower gastrointestinal tract, partially explaining the augmented insulin response after oral compared to i.v. **glucose** administration in normal humans. **GLP-1** also lowers glucagon concns., slows gastric emptying, stimulates (pro)insulin biosynthesis, and reduces food intake upon intracerebroventricular administration in animals. Therefore, **GLP-1** offers some interesting perspective for the treatment of type 2, and perhaps also for type 1 diabetic patients. **GLP-1 glucose** -dependently stimulates insulin secretion in type-2 diabetic patients and exogenous administration of **GLP-1** ([7-37] or [7-36 amide]) in doses elevating plasma concns. to approx. 3-4 times physiol. postprandial levels fully normalizes fasting hyperglycemia and reduces postprandial glycemic increments. Due to rapid proteolytic cleavage, which results in an inactive or even antagonistic fragment, **GLP-1** [9-36 amide], and to rapid elimination, the half-life of **GLP-1** is too short to maintain therapeutic plasma levels for sufficient period by s.c. injections of the natural peptide hormone. Current research aims to characterize **GLP-1** analogs with more suitable pharmacokinetic properties than the original peptide. Given the large amt. of **GLP-1** present in L cells, it also appears worthwhile to search for more agents that could mobilize this endogenous pool of **GLP-1**.

IT **89750-14-1, Glucagon-like peptide 1**

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(**glucagon-like peptide 1** is a potent gut hormone with a possible therapeutic perspective)

L43 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2000 ACS

AN 1998:515987 HCAPLUS

DN 129:211923

TI Relation between gastric emptying of **glucose** and plasma concentrations of **glucagon-like peptide-1**

AU Wishart, Judith M.; Horowitz, Michael; Morris, Howard A.; Jones, Karen L.; **Nauck, Michael A.**

CS Department of Medicine, Royal Adelaide Hospital, Adelaide, 5000, Australia

SO Peptides (N. Y.) (1998), 19(6), 1049-1053
CODEN: PPTDD5; ISSN: 0196-9781

PB Elsevier Science Inc.

DT Journal

LA English

AB **Glucagon-like peptide-1** (**GLP-1**) may play a role in regulating gastric emptying. The aim of this study was to det. the relationship between gastric emptying of **glucose** and plasma concns. of **GLP-1**. Gastric emptying of 75 g of **glucose** dissolved in 350 mL of water was measured by the use of scintigraphy in 12 normal volunteers. Venous blood samples for measurement of **GLP-1** were obtained immediately before and for 180 min after ingestion of **glucose**. Plasma **GLP-1** rose rapidly from a baseline of 8.5 pM to 14.3 pM at 10 min, with a peak of 19.2 pM at 30 min after the **glucose** drink. The rate of gastric emptying was inversely related to the early rise in **GLP-1**, e.g., the 50% emptying time was related to the change in **GLP-1** from baseline at 10 min ($r = 0.57$). The authors conclude that there is an inverse relationship between gastric emptying of **glucose** and plasma **GLP-1**. This observation is consistent with the concept that **GLP-1** is a determinant of, rather than detd. by, the rate of gastric emptying.

IT **50-99-7**, D-**Glucose**, biological studies
89750-14-1, Glucagon-related peptide

I
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(relation between gastric emptying of **glucose** and plasma concns. of **glucagon-like peptide-1** in humans)

L43 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:277998 HCAPLUS
DN 128:290457
TI Overnight **GLP-1** normalizes fasting but not daytime plasma **glucose** levels in NIDDM patients
AU Willms, B.; Idowu, K.; Holst, J. J.; Creutzfeldt, W.; **Nauck, Michael A.**
CS Fachklinik Diabetes Stoffwechselkrankheiten, Bad Lauterberg, Germany
SO Exp. Clin. Endocrinol. Diabetes (1998), 106(2), 103-107
CODEN: ECEDFQ; ISSN: 0947-7349
PB Johann Ambrosius Barth
DT Journal
LA English
AB **Glucagon-like peptide 1** (7-36 amide)**glucagon-like peptide 1** (7-36 amide) (**GLP-1**) normalizes fasting blood plasma **glucose** in NIDDM patients. The effect was studied of overnight i.v. **GLP-1** on the following 24 h-**glucose** profiles. Ten NIDDM patients (7 female, 3 male; age 62 yr., BMI (Body-Mass-Index) 29.6 kg/m2, duration 10 yr., HbA1c 10.9% (normal 4.0-6.1%), treated with glibenclamide and/or metformin) were studied on 2 occasions in random order: either **GLP-1** (Saxon Biochems., Hannover, FRG, 1 pmol/ kg .cntdot.min) or placebo (0.9% NaCl with 1% human serum albumin, Behringwerke, Marburg, FRG) were infused i.v. from 22.00 to 7.00 (9 h) and plasma **glucose** profiles were obtained during the **GLP-1** infusion and the following 24 h. **GLP-1** (plasma concn. 110 pmol/L) raised plasma C-peptide concns., suppressed glucagon, and lowered plasma **glucose** to 5.5 and 6.3 mmol/L at 3.00 and 7.00 a.m. (vs. 10.3 and 11.3 mmol/L, resp., with placebo). Thereafter, starting 1 h after breakfast, no differences in plasma **glucose**, insulin, C-peptide, or glucagon profiles were found between expts. with **GLP-1** and placebo. Plasma **glucose** concns. over the whole 24 h period were reduced by 18% by **GLP-1** administered overnight. In conclusion, (1) overnight **GLP-1** normalizes fasting plasma **glucose**, but (2) has no sustained effect on meal-induced **glucose**, insulin or glucagon concns. once its administration was stopped. (3) Normalization of fasting plasma **glucose** alone does not improve daytime metabolic control in NIDDM patients on oral agents.

L43 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:752513 HCAPLUS
DN 128:44063
TI **Glucagon-like peptide 1** inhibition of gastric emptying outweighs its insulinotropic effects in healthy humans
AU **Nauck, Michael A.**; Niedereichholz, Ulrich; Ettler, Rainer; Holst, Jens Juul; Orskov, Cathrine; Ritzel, Robert; Schmiegel, Wolff H.
CS Department of Medicine, Ruhr-University, Knappschafts-Krankenhaus, Bochum, 044892, Germany
SO Am. J. Physiol. (1997), 273(5, Pt. 1), E981-E988
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB **Glucagon-like peptide 1** (**GLP-1**) has been shown to inhibit gastric emptying of liq. meals in type 2 diabetic patients. It was the aim of the present study to compare the action of physiol. and pharmacol. doses of i.v. **GLP-1**-(7-36) amide and **GLP-1**-(7-37) on gastric emptying in normal volunteers. Nine healthy subjects

participated (26 yr; body mass index 22.9 kg/M2; Hb A1C 5.0%) in five expts. on sep. occasions after an overnight fast. A nasogastric tube was positioned for the detn. of gastric vol. by use of a dye-diln. technique (phenol red). **GLP-1**-(7-36) amide (0.4, 0.8, or 1.2 pmol/kg/min), **GLP-1**-(7-37) (1.2 pmol/kg/min), or placebo was infused i.v. from -30 to 240 min. A liq. meal (50 g sucrose, 8% amino acids, 440 mL, 327 kcal) was administered at 0 min. **Glucose**, insulin, and C-peptide were measured over 240 min. Gastric emptying was dose dependently slowed by **GLP-1**-(7-36) amide. Effects of **GLP-1**-(7-37) at 1.2 pmol/kg/min were virtually identical. **GLP-1** dose dependently stimulated fasting insulin secretion (-30 to 0 min) and slightly reduced **glucose** concns. After the meal (0-240 min), integrated incremental **glucose** and insulin responses were reduced (dose dependently) rather than enhanced. In conclusion, (1) **GLP-1**-(7-36) amide or -(7-37) inhibits gastric emptying also in normal subjects, (2) physiol. doses (0.4 pmol/kg/min) still have a significant effect, (3) despite the known insulinotropic actions of **GLP-1**-(7-36) amide and -(7-37), the net effect of administering **GLP-1** with a meal is no change or a redn. in meal-related insulin responses. These findings suggest a primarily inhibitory function for **GLP-1** (ileal brake mechanisms).

IT **89750-14-1, Glucagon-related peptide I**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**glucagon-like peptide 1** inhibition of gastric emptying outweighs insulinotropic effects in healthy humans)

L43 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:727076 HCAPLUS
DN 127:342096
TI A liquid mixed meal or exogenous **glucagon-like peptide 1** (**GLP-1**) do not alter plasma leptin concentrations in healthy volunteers
AU Drewes, C.; **Nauck, M. A.**; Horn, R.; Holst, J.; Schmiegel, W.; Brabant, G.
CS Knappschafts-Krankenhaus, Univ. Bochum, Bochum, D-44892, Germany
SO Acta Diabetol. (1997), 34(3), 230-234
CODEN: ACDAEZ; ISSN: 0940-5429
PB Springer-Verlag
DT Journal
LA English
AB The role of **glucagon-like peptide 1** [7-36 amide] (**GLP-1**) and the obese gene product (leptin) was investigated in the central regulation of feeding. Blood plasma leptin concns. (31 pmol/L) did not change within 240 min after ingestion of a liq. test meal nor in response to the i.v. infusion of exogenous **GLP-1** leading to plasma levels of 25 and 36 (basal 6) pmol/L. **Glucose** and insulin increased after meal from 4.7 to 6.0 at 15 min and from 28 to 325 pmol/L at 45 min, resp. Plasma leptin levels showed no short-term changes after feeding a liq. mixed meal and did not appear to be directly influenced by physiol. and pharmacol. elevations in plasma **GLP-1**.

IT **89750-14-1, Glucagon-related peptide I**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(no effect of **GLP-1** on blood leptin)

L43 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:687481 HCAPLUS
DN 127:303498

TI **Glucagon-like peptide 1** and its potential in the treatment of non-insulin-dependent diabetes mellitus
AU **Nauck, Michael A.**; Holst, J. J.; Willms, B.
CS Med. Klin., Knappschaftskrankenhaus Bochum, Bochum, D-44892, Germany
SO Horm. Metab. Res. (1997), 29(9), 411-416
CODEN: HMMRA2; ISSN: 0018-5043
PB Thieme
DT Journal
LA English
AB Studies examg. small groups of type 2-(NIDDM) diabetic patients have shown the potential of **glucagon-like peptide 1** (**GLP-1**) to normalize fasting hyperglycemia. Patient characteristics detg. the size of the effect have not been reported. Therefore, the results of four studies were analyzed. Exogenous **GLP-1** was administered i.v. or s.c. in 37 type 2-diabetic patients, age 60 yr; BMI 28.2 kg/m2; HbA1c 10.6 ; diabetes duration 10 yr, treatment with sulfonylureas, n =33, metformin, n =11, acarbose, n = 3. Results were analyzed using repeated measures anal. of variance and multiple regression anal. Exogenous **GLP-1** lowered fasting plasma **glucose** within 4-5 h from 12.8 to 5.3 mmol/L (placebo: 12.8 to 10.0). Only fasting glycemia and the route (i.v. vs. s.c.), but not gender, age, BMI, HbA1c, diabetes duration, treatment with sulfonylureas, metformin, or acarbose, were significant predictors of the plasma **glucose** concns. reached after the administration of **GLP-1** (variation: 3.4-8.5 mmol/L). In conclusion, **GLP-1** is able to normalize plasma **glucose** in all type 2-diabetic patients studied. This anal. underlines the great therapeutic potential of **GLP-1**.
IT **89750-14-1, Glucagon-related peptide I**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glucagon-like peptide 1** and its potential in the treatment of non-insulin-dependent diabetes mellitus)

L43 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:578682 HCAPLUS
DN 127:229715
TI **Glucagonlike peptide** 1
AU **Nauck, Michael A.**
CS Medizinische Universitatsklinik, Knappschafts-Krankenhaus Bochum (Langendreer), Bochum, D 44892, Germany
SO Curr. Opin. Endocrinol. Diabetes (1997), 4(4), 291-299
CODEN: CENDES; ISSN: 1068-3097
PB Rapid Science Publishers
DT Journal; General Review
LA English
AB A review, with 123 refs. **Glucagonlike peptide** 1 is a gut hormone with multiple functions. In addn. to (**glucose**-dependently) stimulating insulin and inhibiting glucagon secretion, it decelerates gastric emptying and enhances (pro)insulin biosynthesis. In addn. to these well-established actions, recent studies suggest an important role in the central regulation of food and water intake and possibly as a minor stimulus to TSH secretion. Further effects on "peripheral" tissues involved in the regulation of carbohydrate metab. (liver, muscle, and adipose tissue) are debated but probably make only minor contributions on the level of the whole organism. The well-preserved activity of **glucagonlike peptide** 1 in type 2 diabetes has led to the suggestion that this hormone or its analogs may be used as new therapeutic agents to reduce or even normalize hyperglycemia in patients with non-insulin dependent diabetes. Redns. in glucagon plasma levels and motility effects are also obsd. in patients with type 1 diabetes, leading to a significant redn. in fasting and postprandial glycemia. A clin. useful prepn. of **glucagonlike peptide** 1, however, has yet to be developed.

IT **89750-14-1, Glucagon-related peptide I**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**Glucagonlike peptide** 1)

L43 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:540016 HCAPLUS
DN 127:215285
TI Glucacon-like peptide 1 (**GLP-1**) as a new therapeutic approach for type 2-diabetes
AU **Nauck, Michael A.**; Holst, J. J.; Willms, B.; Schmiegel, W.
CS Dep. Medicine, Knappschafts-Krankenhaus, Bochum, D-44892, Germany
SO Exp. Clin. Endocrinol. Diabetes (1997), 105(4), 187-195
CODEN: ECEDFQ; ISSN: 0947-7349
PB Barth
DT Journal; General Review
LA English
AB A review with many refs. is given on **glucagon-like peptide 1** (**GLP-1**) as a new therapeutic approach for type 2-diabetes. **GLP-1** is a physiol. incretin hormone in normal humans explaining in part the augmented insulin response after oral vs. i.v. **glucose** administration. In addn., **GLP-1** also lowers glucagon concns., slows gastric emptying, stimulates (pro)insulin biosynthesis, reduces food intake upon intracerebroventricular administration in animals, and may enhance insulin sensitivity. Therefore, **GLP-1** opposes the type 2-diabetic phenotype characterized by disturbed **glucose**-induced insulin secretory capacity, hyperglucagonemia, moderate insulin deficiency, accelerated gastric emptying, overeating (obesity), and insulin resistance. The other incretin hormone, gastric inhibitory polypeptide (GIP), has lost almost all its activity in type 2-diabetic patients. In contrast, **GLP-1** **glucose**-dependently stimulates insulin secretion in diet- and sulfonylurea-treated type 2-diabetic patients and also in patients under insulin therapy long after sulfonylurea 2ndary failure. Exogenous administration of **GLP-1** ([7-37] or [7-36 amide]) in doses elevating plasma concns. to approx. 3-4 fold physiol. postprandial levels fully normalizes fasting hyperglycemia in type 2-diabetic patients. The half life of **GLP-1** is too short to maintain therapeutic blood plasma levels for sufficient periods by s.c. injections. Current research activities aim at finding **GLP-1** analogs with more suitable pharmacokinetic properties than the original peptide. Another approach could be the augmentation of endogenous release of **GLP-1**, which is abundant in L cells of the lower small intestine and the colon. Interference with sucrose digestion using .alpha.-glucosidase inhibition moves nutrients into distal parts of the gastrointestinal tract and, thereby, prolongs and augments **GLP-1** release. Enprostil, a prostaglandin E2 analog, fully suppresses GIP responses, while only marginally affecting insulin secretion and **glucose** tolerance after oral **glucose**, suggesting compensatory hypersecretion of addnl. insulinotropic peptides, possibly including **GLP-1**. Given the large amt. of **GLP-1** present in L cells, it appears worthwhile to look for more agents that could "mobilize" this endogenous pool of the "antidiabetogenic" gut hormone **GLP-1**.

L43 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:509760 HCAPLUS
DN 127:203648
TI The pathogenesis of NIDDM involves a defective expression of the GIP receptor
AU Holst, J. J.; Gromada, J.; **Nauck, M. A.**
CS Dep. Medical Physiology, University Copenhagen, Copenhagen, DK-2200, Den.
SO Diabetologia (1997), 40(8), 984-986
CODEN: DBTGAJ; ISSN: 0012-186X

PB Springer
DT Journal; General Review
LA English
AB A review and discussion with 34 refs., describing decreased incretin effect in non-insulin-dependent diabetes mellitus (NIDDM) patients, full efficacy of **glucagon-like peptide-1** (**GLP-1**) and lack of effect of Glc-dependent insulinotropic polypeptide (GIP) on insulin secretion, and absence of incretin effect (small loads of Glc) at normal GIP secretion in diabetic .beta.-cells. The apparent polygenicity of NIDDM is hypothesized to be caused by genetically defective expression of the GIP receptor.
IT **89750-14-1, Glucagon-related peptide I**
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(the pathogenesis of NIDDM involves a defective expression of the GIP receptor)

L43 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:103399 HCAPLUS
DN 126:181413
TI On the effects of **glucagon-like peptide-1** on blood **glucose** regulation in normal and diabetic subjects
AU Holst, Jens Juul; Toft-Nielsen, Maj-Brit; Oerskov, Cathrine; **Nauck, Michael**; Willms, Behrend
CS Department of Medical Physiology, Panum Institute, University of Copenhagen, Copenhagen, DK-2200, Den.
SO Ann. N. Y. Acad. Sci. (1996), 805(VIP, PACAP, and Related Peptides), 729-736
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal; General Review
LA English
AB A review, with 54 refs.
IT **89750-14-1, Glucagon-related peptide I**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glucagon-like peptide-1** effect on blood **glucose** regulation in normal and diabetic humans)

L43 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:745819 HCAPLUS
DN 126:140060
TI Effects of subcutaneous **glucagon-like peptide 1** (**GLP-1** [7-36 amide]) in patients with NIDDM
AU **Nauck, M. A.**; Wollschlaeger, D.; Werner, J.; Holst, J. J.; Oerskov, C.; Creutzfeldt, W.; Willms, B.
CS Knappschafts-Krankenhaus, Ruhr-Univ., Bochum, D-44892, Germany
SO Diabetologia (1996), 39(12), 1546-1553
CODEN: DBTGAJ; ISSN: 0012-186X
PB Springer
DT Journal
LA English
AB The effects of s.c. administration of **glucagon-like peptide 1** were investigated in non-insulin-dependent diabetic patients. **Glucose**(**glucose** oxidase), insulin, C-peptide, **GLP-1**, and glucagon were measured. Results were similar compared with i.v. infusion in normalizing elevated fasting plasma **glucose** concns. when repeated doses are administered.
IT **89750-14-1, Glucagon-related peptide I**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(s.c. **glucagon-like peptide 1** effect in patients with NIDDM)

L43 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:657992 HCAPLUS
DN 125:293228
TI Potential of **GLP-1** in diabetes management
AU Holst, J. J.; **Nauck, M. A.**; Deacon, C. F.; oerskov, C.
CS Panum Instituttet, University Copenhagen, Copenhagen, 2200, Den.
SO Handb. Exp. Pharmacol. (1996), 123(Glucagon III), 311-326
CODEN: HEPHD2; ISSN: 0171-2004
DT Journal; General Review
LA English
AB A review, with 86 refs., of the insulinotropic activity of **GLP-1** which discusses: actions of **GLP-1** on blood **glucose** in humans; gastrointestinal effects of **GLP-1** in humans; **GLP-1** and diabetes; and **GLP-1** metab. in normal and diabetic subjects.
IT **89750-14-1, Glucagon-related peptide I**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**GLP-1** potential in diabetes management in humans)

L43 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:247447 HCAPLUS
DN 124:333607
TI Release of **glucagon-like peptide 1** (**GLP-1**[7-36 amide]), gastric inhibitory polypeptide (GIP), and insulin in response to oral **glucose** after upper and lower intestinal resections
AU **Nauck, Michael A.**; Siemsgluess, J.; Oerskov, C.; Holst, J. J.
CS Dep. Med., Ruhr-Univ., Bochum, D-44892, Germany
SO Z. Gastroenterol. (1996), 34(3), 159-66
CODEN: ZGASAX; ISSN: 0044-2771
DT Journal
LA English
AB The influence of small intestinal resections or colonectomy on changes in **glucagon-like peptide 1** (GLP) release were investigated after oral **glucose** application in inactive Crohn's disease (no surgery), after primarily jejunal or ileal small intestinal resections, and after 6 colonectomy. Oral **glucose** tolerance tests (75 g) were performed in the fasting state. GLP, insulin, C-peptide, gastric inhibitory peptide (GIP), and glucagon were measured over 240 min. An early (peak: 15-30 min) GLP response was obsd. in all subjects. After colonectomy, higher insulin, C-peptide, and GIP responses were found. Inactive Crohn's disease and resections of the small intestine as well as proctocolectomy did not change GLP response. This may indicate release of GLP after oral **glucose** from the GLP producing L-cells in the upper gut rather than from the ileum, colon, and rectum. Insulin hypersecretion after colonectomy combined with a normal oral **glucose** tolerance possibly indicates a reduced insulin secretion.
IT **50-99-7, D-Glucose**, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(release of **glucagon-like peptide 1** (**GLP-1**[7-36 amide]), gastric inhibitory polypeptide, and insulin in response to oral **glucose** after upper and lower intestinal resections)

L43 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:48902 HCAPLUS
DN 124:107246
TI Gastric emptying, **glucose** responses, and insulin secretion after a liquid test meal: effects of exogenous **glucagon-like peptide-1** (**GLP-1**)-(7-36) amide in

type 2 (noninsulin-dependent) diabetic patients
AU Willms, Berend; Werner, Jens; Holst, Jens Juul; Oerskov, Cathrine; Creutzfeldt, Werner; **Nauck, Michael A.**
CS Fachklinik Diabetes und Stoffwechselkrankheiten, Bad Lauterberg, Germany
SO J. Clin. Endocrinol. Metab. (1996), 81(1), 327-32
CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB The aim of the study was to investigate whether inhibition of gastric emptying of meals plays a role in the mechanism of the blood **glucose**-lowering action of **glucagon-like peptide-1**-(7-36) amide [**GLP-1**-(7-36) amide] in type 2 diabetes. Eight poorly controlled type 2 diabetic patients (age, 58 .+-. 6 yr; body mass index, 30.0 .+-. 5.2 kg/m2; Hb A1c, 10.5 .+-. 1.2%) were studied in the fasting state (plasma **glucose**, 11.1 .+-. 1.1 mmol/L). A liq. meal of 400 mL contg. 8% amino acids and 50 g sucrose (327 kcal) was administered at time zero by a nasogastric tube. Gastric vol. was detd. by a dye diln. technique using phenol red. In randomized order, **GLP-1**-(7-36) amide (1.2 pmol/kg.cntdot.min; Saxon Biochems.) or placebo (0.9% NaCl with 1% human serum albumin) was infused between -30 and 240 min. In the control expt., gastric emptying was completed within 120 min, and plasma **glucose**, insulin, C-peptide, **GLP-1**-(7-36) amide, and glucagon concns. transiently increased. With exogenous **GLP-1**-(7-36) amide (plasma level, .apprx.70 pmol/L), gastric vol. remained const. over the period it was measured (120 min; $P < 0.0001$ vs. placebo), and plasma **glucose** fell to normal fasting values (5.4 .+-. 0.7 nmol/L) within 3-4 h, whereas insulin was stimulated in most, but not all, patients, and glucagon remained at the basal level or was slightly suppressed. In conclusion, **GLP-1**-(7-36) amide inhibits gastric emptying in type 2 diabetic patients. Together with the stimulation of insulin and the inhibition of glucagon secretion, this effect probably contributes to the blood **glucose**-lowering action of **GLP-1**-(7-36) amide in type 2-diabetic patients when studied after meal ingestion. At the degree obsd., inhibition of gastric emptying, however, must be overcome by tachyphylaxis, redn. in dose, or pharmacol. interventions so as not to interfere with the therapeutic use of **GLP-1**-(7-36) amide in type 2 diabetic patients.

L43 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:952161 HCAPLUS
DN 124:1186
TI **Glucagon-like peptide 1** (7-36 amide) secretion in response to luminal sucrose from the upper and lower gut: A study using .alpha.-glucosidase inhibition (acarbose)
AU Qualmann, C.; **Nauck, M. A.**; Holst, J. J.; Orskov, C.; Creutzfeldt, W.
CS Dept. Medicine, Georg-August University, Goettingen, Germany
SO Scand. J. Gastroenterol. (1995), 30(9), 892-6
CODEN: SJGRA4; ISSN: 0036-5521
DT Journal
LA English
AB After nutrient ingestion there is an early response of **glucagon-like peptide 1** (**GLP-1**) immunoreactivity, although **GLP-1** is mainly produced in endocrine cells from the lower gut (ileum and colon/rectum), suggesting that indirect stimulation is important after the ingestion of carbohydrates that are predominantly absorbed from the upper intestine. To enable contact of sucrose with lower gut mucosa, sucrose was administered by mouth with and without the simultaneous ingestion of 100 mg of the .alpha.-glucosidase inhibitor acarbose to six normal healthy volunteers. There was an early increase in **GLP-1** 15 min after sucrose ingestion. With acarbose, sucrose reached the colon approx. 120 min after ingestion, as indicated by an increase in breath hydrogen exhalation, and **GLP-1** release was prolonged. The sucrose-related increases in **glucose**, insulin, C-peptide,

and gastric inhibitory polypeptide (GIP) and the suppression of glucagon were only marginally affected by acarbose administration. Thus, **GLP-1** release appears to be influenced by indirect mechanisms (early response after sucrose) and by direct luminal contact with lower gut mucosal endocrine cells (late response with acarbose).

L43 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:660255 HCAPLUS
DN 123:103130
TI Pharmacokinetic, insulinotropic, and glucagonostatic properties of **GLP-1** [7-36 amide] after subcutaneous injection in healthy volunteers. Dose-response-relationships
AU Ritzel, R.; Oerskov, C.; Holst, J.J.; **Nauck, M.A.**
CS Department of Medicine, Ruhr-University, Bochum, D-44892, Germany
SO Diabetologia (1995), 38(6), 720-5
CODEN: DBTGAJ; ISSN: 0012-186X
DT Journal
LA English
AB I.v. infusions of **glucagon-like peptide 1** (**GLP-1**) [7-36 amide] are **glucose**-dependently insulinotropic and glucagonostatic and normalize plasma **glucose** concns. in non-insulin-dependent diabetic patients. It was the aim of this study to investigate whether s.c. **GLP-1** [7-36 amide] also has an influence on insulin and glucagon secretion, and which doses are required for significant effects. Therefore, eight healthy volunteers (24 .+-. 2 yr, body mass index [BMI] 21.9 .+-. 2.3 kg/m2) were studied in the fasting state on five occasions in randomized order. Placebo (0.9% NaCl with 1 % human serum albumin) or **GLP-1** [7-36 amide] in doses of 0.15, 0.5, 1.5 or 4.5 nmol/kg body wt. (vol. 1 mL or, at the highest dose, 2 mL) was administered s.c. An i.v. **glucose** bolus (0.33 g/kg body wt.) was injected 30 min later. Blood was drawn for the measurement of **glucose**, insulin, C-peptide, **GLP-1** [7-36 amide], and glucagon using specific RIAs. There were dose-related increments in **GLP-1** [7-36 amide] concns. ($p < 0.0001$). However, basal values were reached again after 90-120 min. Before **glucose** administration, insulin ($p < 0.0001$) and C-peptide ($p < 0.0004$) increased, whereas glucagon ($p = 0.0018$) and **glucose** ($p < 0.0001$) decreased in a dose-dependent manner. After **glucose** stimulation, integrated increments in insulin ($p = 0.0007$) and C-peptide ($p = 0.02$) were augmented and KG-values increased ($p < 0.0001$) in a dose-related fashion. The extent of reactive hypoglycemia was related to the **GLP-1** [7-36 amide] dose. With the highest **GLP-1** [7-36 amide] dose, at the time of peak plasma concns., most volunteers felt unwell, and nausea and vomiting were obsd. in four subjects. In conclusion, s.c. **GLP-1** [7-36 amide] is also able to stimulate insulin and inhibit glucagon secretion, thereby altering **glucose** assimilation. However, with unmodified **GLP-1** [7-36 amide], the duration of action is short, and with high doses side effects are common.
IT **89750-14-1**, **Glucagon-related peptide I**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
((**GLP-1**) [7-36 amide]; pharmacokinetic, insulinotropic, and glucagonostatic properties of **GLP-1** [7-36 amide] after s.c. injection in healthy volunteers. Dose-response-relationships)
IT **50-99-7**, D **Glucose**, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(pharmacokinetic, insulinotropic, and glucagonostatic properties of **GLP-1** [7-36 amide] after s.c. injection in healthy volunteers. Dose-response-relationships)

L43 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2000 ACS

AN 1995:627109 HCAPLUS
DN 123:26026
TI Insulinotropic actions of intravenous **glucagon-like peptide-1** (**GLP-1**) [7-36 amide] in the fasting state in healthy subjects
AU Qualmann, C.; **Nauck, M. A.**; Holst, J. J.; Oerskov, C.; Creutzfeldt, W.
CS Department of Medicine, Georg-August-University, Goettingen, Germany
SO Acta Diabetol. (1995), 32(1), 13-16
CODEN: ACDAEZ; ISSN: 0940-5429
DT Journal
LA English
AB **GLP-1** (7-36 amide) stimulates insulin and suppresses glucagon secretion in normal subjects and may, in pharmacol. doses, normalize hyperglycemia in type 2 diabetic patients. It is not known whether such pharmacol. doses can actually lower blood **glucose** to hypoglycemic levels. Therefore, in seven normal fasting subjects, **GLP-1** (7-36 amide) was infused i.v. at 0.3, 0.9 and 2.7 pmol/kg per min for 30 min each. The plasma concn. of **GLP-1** (7-36 amide) increased dose-dependently, but insulin secretion (insulin, C-peptide) was stimulated only marginally. Glucagon was slightly suppressed, and plasma **glucose** was reduced, but not into the hypoglycemic range. In conclusion, when plasma **glucose** concns. are in the normal fasting range, **GLP-1** (7-36 amide) is not able to stimulate insulin secretion to a degree that causes hypoglycemia. This should limit the risk of hypoglycemic responses when **GLP-1** (7-36 amide) is administered in pharmacol. doses to reduce hyperglycemia in type 2 diabetic patients.
IT **50-99-7**, D-**Glucose**, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**glucagon-like peptide-1** effect on plasma **glucose** in humans)

L43 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:582099 HCAPLUS
DN 122:306962
TI Physiological augmentation of amino acid-induced insulin secretion by GIP and **GLP-I** but not by CCK-8
AU Fieseler, Pia; Bridenbaugh, Stephanie; Nustede, Rainer; Martell, Joachim; Orskov, Cathrine; Holst, Jens J.; **Nauck, Michael A.**
CS Georg-August Univ., Goettingen, D-37075, Germany
SO Am. J. Physiol. (1995), 268(5, Pt. 1), E949-E955
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English
AB It was the aim of this study to test insulinotropic actions of cholecystokinin octapeptide (CCK-8), gastric inhibitory polypeptide (GIP), and **glucagon-like peptide I** (**GLP-I**)-(7-36) amide at basal **glucose** but physiol. elevated amino acid concns. Therefore, in nine fasting healthy volunteers, an amino acid mixt. was infused i.v. (12.6 g/h over 120 min). On sep. occasions, from 30 to 120 min, placebo (0.9% NaCl-1% human serum albumin), synthetic sulfated CCK-8 (0.5 pmol.cntdot.kg-1.cntdot.min-1), human GIP (1 pmol.cntdot.kg-1.cntdot.min-1), or **GLP-I**-(7-36) amide (0.3 pmol.cntdot.kg-1.cntdot.min-1) was infused i.v. to mimic physiol. increments after a meal. The amino acid infusion lead to a small increment in plasma **glucose** from 4.8 to 5.0 mmol/1 and significantly elevated insulin and C-peptide concns. GIP and **GLP-I**-(7-36) amide further stimulated insulin (1.8-fold, and 0.004, resp.) and C-peptide (1.3-fold, and 0.013, resp.), with a subsequent slight redn. in plasma **glucose**. Insulin and C-peptide then decreased again in parallel. CCK-8 was without effect on insulin and C-peptide levels. In conclusion, GIP and **GLP-I**-(7-36) amide are not only able to interact with elevated plasma **glucose** but are insulinotropic also with physiol. raised amino acid concns. Such an interaction could play a role after the ingestion of mixed meals.

Cholecystokinin, is not a physiol. incretin also under these conditions.

L43 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1993:420852 HCAPLUS
DN 119:20852
TI Additive insulinotropic effects of exogenous synthetic human gastric inhibitory polypeptide and **glucagon-like peptide-1**-(7-36) amide infused at near-physiological insulinotropic hormone and **glucose** concentrations
AU **Nauck, Michael A.**; Bartels, Eckart; Oerskov, Catherine; Ebert, Reinhold; Creutzfeldt, Werner
CS Dep. Med., Georg August Univ., Goettingen, Germany
SO J. Clin. Endocrinol. Metab. (1993), 76(4), 912-17
CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB Gastric inhibitory polypeptide (GIP) and **glucagon-like peptide-1**-(7-36) amide (**GLP-1**) are **glucose**-dependent insulinotropic gut hormones that may explain the greater insulin secretory response with oral compared to i.v. **glucose** (incretin effect). To study their individual and combined contributions, in 8 healthy volunteers, on sep. occasions, synthetic human GIP (1 pmol/kg/min) and/or **GLP-1** (0.3 pmol/kg.min) or placebo were infused i.v. (-30 to 120 min), while at 0 min, a **glucose** infusion isoglycemic to the profile after an oral **glucose** load of 50 g/400 mL was started. After the administration of 50 g oral **glucose**, immunoreactive GIP rose several-fold to 337 pmol/L, while there was only a transient (10-30 min) and moderate increment in immunoreactive **GLP-1** (from basal, 25-30, to 41 pmol/L). Isoglycemic i.v. **glucose** infusions led to smaller B-cell responses (estd. incretin effect, 41%). With single infusions of GIP or **GLP-1** (circulating concns., 464 and 54 pmol/L, resp.), B-cell responses were augmented compared to i.v. **glucose** alone and were no longer different from those after oral **glucose**. The combination of GIP and **GLP-1** led to B-cell responses that were higher than those with either hormone alone (additive mode of cooperation). Plasma GIP concns. were similar after endogenous secretion (oral **glucose**) and i.v. infusion, while exogenously administered **GLP-1** led to plasma levels that were maintained at an elevated level for a longer period during exogenous infusion than after stimulation by oral **glucose**. When in 7 volunteers, a lower dose (0.15 pmol/kg.min) of **GLP-1** was infused during isoglycemic **glucose** infusion expts. only for the duration of elevated plasma levels in the oral **glucose** challenges (0-30 min), a transient, increment in insulin and C-peptide concns. was obsd., which was equiv. to 26% of the estd. incretin effect. Circulating GIP seems to make a major contribution to the incretin effect after oral **glucose**, and **GLP-1** appears to mediate a smaller proportion. GIP and **GLP-1** can interact in an additive manner in normal man.
IT **50-99-7**, D-**Glucose**, biological studies
RL: BIOL (Biological study)
(insulin secretion response to, in human, gastric inhibitory polypeptide and **glucagon-like peptide 1** effect on)

L43 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2000 ACS
AN 1993:16644 HCAPLUS
DN 118:16644
TI Lack of effect of synthetic human gastric inhibitory polypeptide and **glucagon-like peptide 1** [7-36 amide] infused at near-physiological concentrations on pentagastrin-stimulated gastric acid secretion in normal human subjects
AU **Nauck, Michael A.**; Bartels, Eckart; Oerskov, Cathrine; Ebert, Reinhold; Creutzfeldt, Werner
CS Dep. Med., Georg-August-Univ., Goettingen, Germany

SO Digestion (1992), 52(3-4), 214-21
CODEN: DIGEBW; ISSN: 0012-2823
DT Journal
LA English
AB Gastric inhibitory polypeptide (GIP) and **glucagon-like peptide 1** [7-36 amide] (**GLP-1**) are **glucose**-dependent insulinotropic gut hormones. Under exptl. conditions, both have been shown to reduce stimulated gastric acid secretion. To study their individual and combined effects on pentagastrin-stimulated (0.1 .mu.g/kg/h from -90 to 120 min) gastric vol. and acid and chloride outputs, on sep. occasions, synthetic human GIP (1 pmol/kg/min) and/or **GLP-1** [7-36 amide] (0.3 pmol/kg/min) or placebo (0.9% NaCl with 1% albumin) were infused i.v. (from -30 to 120 min) into 9 healthy volunteers. At 0 min, a **glucose** infusion was started that mimicked the glycemic profile after an oral **glucose** load of 50 g/400 mL and allowed for the **glucose**-dependent insulinotropic action of GIP and **GLP-1** [7-36 amide]. Pentagastrin stimulated acid output significantly, but neither GIP nor **GLP-1** [7-36 amide] either alone or in combination, reduced pentagastrin-stimulated gastric acid secretion. The circulating concns. of GIP and **GLP-1** [7-36 amide] obtained at steady state during exogenous administration of synthetic peptides were similar to or higher than those reached after oral **glucose** (endogenous secretion). In conclusion, (penta)gastrin-stimulated gastric acid secretion is not inhibited by physiol. circulating concns. of GIP or **GLP-1** [7-36 amide]. Therefore, the insulinotropic action of these intestinal hormones is physiol. more important than their possible role as enterogastrone.

=> fil biosis

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E NAUCK M/AU
L44 151 S E3,E4,E10-E12
E WAGNER F/AU
L45 262 S E3,E33,E36,E38
L46 217396 S L9,L11,L13 OR GLUCOSE
L47 1908 S L20
L48 1433 S L30
L49 1336 S L46 AND L47,L48
L50 12 S L49 AND PARENTER?
L51 3 S L50 NOT AB/FA
L52 2050 S L47 OR GASTRIC INHIBITORY () (PEPTIDE OR POLYPEPTIDE OR POLY
L53 1191 S L22 OR (GLUCAGON OR GLUCACON)()(LIKE OR RELATED)()(PEPTIDE OR
L54 1351 S L46 AND L52,L53

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L55          12 S L54 AND PARENTER?
L56           3 S L55 NOT AB/FA
L57           0 S L55 AND COMPOSITION
L58          15 S L54 AND COMPOSITION
L59           1 S L58 AND (7()36)/TI
L60         468 S L54 AND 132?/CC
L61         398 S L60 AND PY<=1995
L62         100 S L61 AND 125?/CC
L63           8 S L61 AND COMPOS?
L64          20 S L61 AND 7()(34 OR 35 OR 36 OR 37)
L65           2 S L64 AND INTRADUODEN?
L66          90 S L44,L45 AND L46
L67          41 S L66 AND L54
L68          23 S L67 AND PY<=1995
L69          26 S L59,L65,L68
L70           8 S L69 AND 00520/CC
L71           8 S L69 AND (CONFERENC? OR CONGRESS? OR POSTER? OR SYMPOS? OR MEE
L72           9 S L70,L71,L59,L65

     FILE 'BIOSIS' ENTERED AT 13:32:40 ON 10 APR 2000

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L72  ANSWER 1 OF 9  BIOSIS  COPYRIGHT 2000 BIOSIS
AN   1997:427863  BIOSIS
DN   PREV199799727066
TI   Plasma glucagon-like peptide-1 (
     7-36) amide (GLP-1) response in healthy volunteers to
     liquid phase, solid phase and meals of differing lipid composition
     .
AU   Brynes, Audrey E.; Frost, Gary S.; Edwards, C. Mark B.; Ghatei, Mohammad
     A.; Bloom, Stephen R.
CS   Dep. Nutrition and Dietics, Hammersmith Hosp., London W12 0HS UK
SO   Proceedings of the Nutrition Society, (1997) Vol. 56, No. 2, pp.
     224A.
     Meeting Info.: Joint Meeting of the Clinical Nutrition and Metabolism
     Group of the Nutrition Society and the British Association for Parenteral
     and Enteral Nutrition Blackpool, England, UK December 3-5, 1996
     ISSN: 0029-6651.
DT   Conference; Abstract
LA   English
CC   General Biology - Symposia, Transactions and Proceedings of
     Conferences, Congresses, Review Annuals   00520
     Biochemical Studies - Proteins, Peptides and Amino Acids  *10064
     Metabolism - Proteins, Peptides and Amino Acids  *13012
     Nutrition - General Studies, Nutritional Status and Methods  *13202
     Nutrition - General Dietary Studies  *13214
     Nutrition - Lipids   *13222
     Digestive System - Physiology and Biochemistry  *14004
     Endocrine System - Pancreas  *17008
BC   Hominidae  *86215
IT   Major Concepts
        Biochemistry and Molecular Biophysics; Digestive System (Ingestion and
        Assimilation); Endocrine System (Chemical Coordination and
        Homeostasis); Metabolism; Nutrition
IT   Chemicals & Biochemicals
        GLUCAGON; INSULIN; GLUCOSE
IT   Miscellaneous Descriptors
        DIGESTIVE SYSTEM; ENDOCRINE SYSTEM; GLUCAGON-LIKE
      PEPTIDE-1; GLUCOSE; INSULIN; LIPID; LIQUID
        MEAL; MEAL LIPID COMPOSITION; NUTRITION; PLASMA; SOLID MEAL
ORGN Super Taxa
        Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
        human (Hominidae)
```

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 9007-92-5 (GLUCAGON)
9004-10-8 (INSULIN)
50-99-7 (GLUCOSE)

L72 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:424763 BIOSIS
DN PREV199598439063
TI **Glucagon-like peptide 1** (7-36 amide) lowers blood **glucose** also in type-1-diabetic patients.
AU Willms, B. (1); Kleine, Nicola; Creutzfeldt, W.; Orskov, C.; Holst, J.; **Nauck, M.**
CS (1) Bad Lauterberg im Harz, Goettingen Germany
SO Diabetologia, (1995) Vol. 38, No. SUPPL. 1, pp. A40.
Meeting Info.: **31st Annual Meeting of the European Association for the Study of Diabetes** Stockholm, Sweden September 12-16, 1995
ISSN: 0012-186X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Carbohydrates *10068
Metabolism - Carbohydrates *13004
Metabolism - Metabolic Disorders *13020
Endocrine System - Pancreas *17008
BC Hominidae *86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Endocrine System (Chemical Coordination and Homeostasis); Metabolism
IT Chemicals & Biochemicals
GLUCAGON; AMIDE; **GLUCOSE**
IT Miscellaneous Descriptors
MEETING ABSTRACT
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 9007-92-5 (GLUCAGON)
17655-31-1 (AMIDE)
50-99-7 (GLUCOSE)

L72 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:218176 BIOSIS
DN PREV199598232476
TI **Glucagon-like peptide-1** and **glucose**-dependent insulin-releasing polypeptide plasma levels in response to nutrients.
AU Herrmann, Christine; Goeke, Ruediger; Richter, Gerd; Fehmann, Hans-C.; Arnold, Rudolf; Goeke, Burkhard (1)
CS (1) Clin. Res. Unit. Gastrointestinal Endocrinol., Dep. Intern. Med., Philipps Univ. Marburg, Baldingerstrasse, D-35033 Marburg Germany
SO Digestion, (1995) Vol. 56, No. 2, pp. 117-126.
ISSN: 0012-2823.
DT Article
LA English
AB The nutrient-dependent **glucagon-like peptide -1** (**7-36**) amide (GLP-1 release was studied in comparison to the **glucose**-dependent insulin-releasing polypeptide (**GIP**) response in 10 healthy volunteers each undergoing various protocols. Plasma samples were saved up to 120 min after challenges by oral, intravenous or **intraduodenal** administration of nutrients. Basal plasma-GLP-1 concentrations ranged

between 0.4 and 1.4 pM, maximal postprandial GLP-1 levels peaked between 10 and 12 pM. Intravenous **glucose** (25 g i.v.) did not change basal GLP-1 levels. Oral administration of **glucose** (50 g) induced a biphasic GLP-1 release peaking at 30-60 min and a biphasic **GIP** release peaking at 5 and 45 min. This increase paralleled the secretion of insulin. Oral galactose (100 g) and amino acids (25 g) also induced a rapid plasma GLP-1 response. After fat (67 g corn oil) a strong and long-lasting (gt 120 min) increase of GLP-1 plasma levels occurred. When a mixed liquid meal was given (6 g soybean oil, 5 g casein, 13 g **glucose**) immunoreactive (IR)-GLP-1 rapidly increased and peaked after 5 min with declining levels after 30 min. In response to an **intraduodenal** infusion of a small **glucose** load (5.34 g within 120 min) a rapid, short-lasting GLP-1 response occurred whereas plasma **GIP** and insulin levels remained unaltered. Luminal perfusion of an isolated vascularly perfused rat ileum with a polydiet induced a rapid rise of portally released IR-GLP- 1 which was followed by a sustained release. **Glucose** evoked sodium-dependently a sharp increase of IR-GLP-1 levels followed by a plateau release. The intraluminal infusion of a mixture of amino acids or fat was without any effect on IR-GLP-1. We hypothesize that in contrast to **GIP** the GLP-1 release from L cells is triggered by nervous reflexes, by putative humoral factor(s) being released from the upper small intestine in addition to nutrient stimuli acting at the luminal surface of the gut.

CC Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Nutrition - General Studies, Nutritional Status and Methods *13202
Digestive System - Physiology and Biochemistry *14004
Endocrine System - Pancreas *17008
Endocrine System - Neuroendocrinology *17020
Nervous System - Physiology and Biochemistry *20504
BC Hominidae *86215
IT Major Concepts
Cell Biology; Digestive System (Ingestion and Assimilation); Endocrine System (Chemical Coordination and Homeostasis); Nervous System (Neural Coordination); Nutrition
IT Chemicals & Biochemicals
GLUCAGON; **GLUCOSE**; INSULIN
IT Miscellaneous Descriptors
GASTRIC INHIBITORY PEPTIDE; L-CELL
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 9007-92-5 (GLUCAGON)
50-99-7 (GLUCOSE)
9004-10-8 (INSULIN)

L72 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:93920 BIOSIS
DN PREV199598108220
TI **GIP** and GLP-1(**7-36**)amide secretion in response to **intraduodenal** nutrient infusions in pigs.
AU Knapper, J. M. E. (1); Morgan, L. M. (1); Fletcher, J. M.; Marks, V. (1)
CS (1) Nutritional Metabolism Research Group, Sch. Biol. Sci., Univ. Surrey, Guildford GU2 5XH UK
SO **Proceedings of the Nutrition Society**, (1994) Vol. 53, No. 3, pp. 228A.
Meeting Info.: **Scientific Meeting of the Nutrition Society** Southampton, England, UK August 2-5, 1994
ISSN: 0029-6651.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of**

Conferences, Congresses, Review Annuals 00520
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066
Biochemical Studies - Carbohydrates 10068
Biophysics - Molecular Properties and Macromolecules *10506
Movement *12100
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Nutrition - General Studies, Nutritional Status and Methods *13202
Nutrition - General Dietary Studies *13214
Nutrition - Carbohydrates *13220
Nutrition - Lipids *13222
Nutrition - Proteins, Peptides and Amino Acids *13224
Digestive System - General; Methods *14001
Digestive System - Physiology and Biochemistry *14004
Endocrine System - General *17002
Endocrine System - Pancreas *17008
Routes of Immunization, Infection and Therapy *22100
BC Suidae *85740
IT Major Concepts
Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation); Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Methods and Techniques; Nutrition; Physiology
IT Chemicals & Biochemicals
GLUCOSE; GLUCAGON
IT Miscellaneous Descriptors
CARBOHYDRATE; FAT; **GLUCAGON-LIKE PEPTIDE 1** ACTIVE TRUNCATED FORM; **GLUCOSE-DEPENDENT INSULINOTROPIC POLYPEPTIDE**; GUT HORMONE SECRETION; **MEETING ABSTRACT**; POSTPRANDIAL METABOLISM
ORGN Super Taxa
Suidae: Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Suidae (Suidae)
ORGN Organism Superterms
animals; artiodactyls; chordates; mammals; nonhuman vertebrates; nonhuman mammals; vertebrates
RN **50-99-7 (GLUCOSE)**
9007-92-5 (GLUCAGON)

L72 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:462728 BIOSIS
DN PREV199497475728
TI Release of GLP-1 (7-36 amide) after oral **glucose** in relation to **glucose** tolerance and sex.
AU **Nauck, M. (1)**; Erpenstein, A.; Holst, J. J.; Orskov, C.; Von Boxberg, C.; Wirtz, G.; Tillil, H.; Koebberling, J.; Creutzfeldt, W.
CS (1) Bochum Germany
SO Diabetologia, (1994) Vol. 37, No. SUPPL. 1, pp. A118.
Meeting Info.: **30th Annual Meeting of the European Association for the Study of Diabetes** Duesseldorf, Germany September 27-October 1, 1994
ISSN: 0012-186X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Genetics and Cytogenetics - Sex Differences *03510
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Pathology, General and Miscellaneous - Diagnostic *12504
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Metabolic Disorders *13020

Digestive System - Physiology and Biochemistry *14004
Endocrine System - Pancreas *17008
Pharmacology - Clinical Pharmacology *22005
Pharmacology - Endocrine System *22016
BC Hominidae *86215
IT Major Concepts
Digestive System (Ingestion and Assimilation); Endocrine System (Chemical Coordination and Homeostasis); Genetics; Metabolism; Pathology; Pharmacology
IT Chemicals & Biochemicals
AMIDE; **GLUCOSE**; GLUCAGON
IT Miscellaneous Descriptors
DIABETES; DIAGNOSTIC-DRUG; **GLUCAGON-LIKE PEPTIDE I**; **GLUCOSE**; **MEETING ABSTRACT**; **MEETING POSTER**
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 17655-31-1 (AMIDE)
50-99-7 (**GLUCOSE**)
9007-92-5 (GLUCAGON)

L72 ANSWER 6 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:102263 BIOSIS
DN PREV199497115263
TI Normalization of fasting hyperglycaemia by exogenous **glucagon-like peptide 1**(7-36)amide in type 2 (non-insulin-dependent) diabetic patients.
AU **Nauck, M. A. (1)**; Kleine, N.; Orskov, C.; Holst, J. J.; Willms, B.; Creutzfeldt, W.
CS (1) Div. Gastroenterol. and Endocrinol., Dep. Med., Georg August Univ., D-37073 Goettingen Germany
SO Digestion, (1993) Vol. 54, No. 6, pp. 389.
Meeting Info.: **International Symposium on Glucagon-Like Peptide-1** Copenhagen, Denmark May 17-19, 1993
ISSN: 0012-2823.
DT Article
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Carbohydrates *13004
Metabolism - Metabolic Disorders *13020
Digestive System - Physiology and Biochemistry *14004
Endocrine System - Pancreas *17008
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Clinical Pharmacology *22005
BC Hominidae *86215
IT Major Concepts
Digestive System (Ingestion and Assimilation); Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Pathology; Pharmacology
IT Chemicals & Biochemicals
METFORMIN; ACARBOSE; INSULIN; C PEPTIDE; GLUCAGON; **GLUCOSE**; INCRETIN
IT Miscellaneous Descriptors
ACARBOSE; ANTIDIABETIC-DRUG; C PEPTIDE; GLUCAGON; **GLUCOSE**; HYPERGLYCEMIA; INCRETIN HORMONE; INSULIN; METABOLIC-DRUG; METFORMI SULFONYLUREA; THERAPY
ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 657-24-9 (METFORMIN)
56180-94-0 (ACARBOSE)
9004-10-8 (INSULIN)
59112-80-0 (C PEPTIDE)
9007-92-5 (GLUCAGON)
50-99-7 (GLUCOSE)
54241-84-8 (INCRETIN)

L72 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:1376 BIOSIS
DN PREV199497014376
TI Insulinotropic actions of **GIP** and GLP-1 (7-36 amide), but not of CCK-8 at physiologically elevated amino acid concentrations.
AU **Nauck, M. A. (1)**; Fieseler, P.; Orskov, C.; Holst, J. J.; Nustede, R.; Martell, J.
CS (1) Dep. Med., Georg-August-Univ., Goettingen Germany
SO Diabetologia, (1993) Vol. 36, No. SUPPL. 1, pp. A48.
Meeting Info.: **29th Annual Meeting of the European Association for the Study of Diabetes** Istanbul, Turkey September 6-10, 1993
ISSN: 0012-186X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Metabolism - Proteins, Peptides and Amino Acids *13012
Nutrition - Proteins, Peptides and Amino Acids *13224
Digestive System - Physiology and Biochemistry *14004
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Endocrine System - Pancreas *17008
Endocrine System - Neuroendocrinology *17020
Nervous System - Physiology and Biochemistry *20504
BC Hominidae *86215
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Digestive System (Ingestion and Assimilation); Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Nervous System (Neural Coordination); Nutrition
IT Chemicals & Biochemicals
AMIDE; CCK-8; CHOLECYSTOKININ-8; GLUCAGON; **GLUCOSE**
IT Miscellaneous Descriptors
CHOLECYSTOKININ-8; GLUCAGON-LIKE INSULINOTROPIC PEPTIDE; **GLUCAGON-LIKE PEPTIDE 1**; **MEETING ABSTRACT**; PANCREATIC GLUCAGON; PLASMA **GLUCOSE** ; PROTEIN MEAL
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 17655-31-1 (AMIDE)
25126-32-3 (CCK-8)
25126-32-3 (CHOLECYSTOKININ-8)
9007-92-5 (GLUCAGON)
50-99-7 (GLUCOSE)

L72 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1991:536190 BIOSIS

DN BR41:125925
TI INSULINOTROPHIC EFFECTS OF A COMBINATION OF HUMAN SYNTHETIC **GIP** AND GLP-1 7-36 AMIDE AT PHYSIOLOGICAL PLASMA **GLUCOSE** IN MAN.
AU **NAUCK M**; BARTELS E; ORSKOV C; EBERT R; CREUTZFELDT W
CS DEP. MED., GEORG-AUGUST-UNIV., GOETTINGEN, GER.
SO 27TH ANNUAL **MEETING** OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES, DUBLIN, IRELAND, SEPTEMBER 10-14, 1991. DIABETOLOGIA. (1991) 34 (SUPPL 2), A14.
CODEN: DBTGAJ. ISSN: 0012-186X.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Methods - Proteins, Peptides and Amino Acids 10054
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Metabolism - Carbohydrates 13004
Metabolism - Metabolic Disorders 13020
Digestive System - Physiology and Biochemistry *14004
Endocrine System - General *17002
Endocrine System - Pancreas *17008
Immunology and Immunochemistry - General; Methods 34502
BC Hominidae 86215
IT Miscellaneous Descriptors
ABSTRACT GASTRIC INHIBITORY PEPTIDE GLUCAGON LIKE PEPTIDE DIABETES DIABETES MELLITUS RADIOIMMUNOASSAY
RN **50-99-7** (**GLUCOSE**)
17655-31-1 (AMIDE)
96352-57-7 (GLUCAGON LIKE PEPTIDE)

L72 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1988:476775 BIOSIS
DN BR35:106665
TI INSULINOTROPIC ACTIVITY OF SYNTHETIC HUMAN **GIP** IN MAN.
AU **NAUCK M**; STRIETZEL J; EBERT R; CREUTZFELDT W
CS DIV. GASTROENTEROL. ENDOCRINOL., DEP. MED., UNIV. GOETTINGEN, GOETTINGEN, FRG.
SO 24TH ANNUAL **MEETING** OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES, PARIS, FRANCE, SEPTEMBER 5-8, 1988. DIABETOLOGIA. (1988) 31 (7), 525A.
CODEN: DBTGAJ. ISSN: 0012-186X.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Clinical Biochemistry; General Methods and Applications *10006
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Endocrine System - Pancreas *17008
Dental and Oral Biology - General; Methods 19001
BC Hominidae 86215
IT Miscellaneous Descriptors
ABSTRACT GLUCOSE-DEPENDENT INSULINOTROPIC POLYPEPTIDE ORAL **GLUCOSE**
RN **50-99-7** (**GLUCOSE**)

=> fil embase

FILE 'EMBASE' ENTERED AT 13:43:41 ON 10 APR 2000

FILE COVERS 1974 TO 6 Apr 2000 (20000406/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

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=> d his l73-

(FILE 'BIOSIS' ENTERED AT 13:12:16 ON 10 APR 2000)

FILE 'BIOSIS' ENTERED AT 13:32:40 ON 10 APR 2000

FILE 'EMBASE' ENTERED AT 13:32:58 ON 10 APR 2000

```
L73      168442 S L46
L74        2534 S L52 OR L53
L75        2734 S L74 OR (GLUCAGON OR GLUCACON)()LIKE()(PEPTIDE OR POLYPEPTIDE
L76        1308 S L73 AND L75
L77          16 S L76 AND ?PARENTERAL?
L78          12 S L77 AND PY<=1995
L79           2 S L78 AND (PROLONGED)/TI
                E NAUCK M/AU
L80         133 S E3,E4
                E WAGNER F/AU
L81         208 S E3,E4
L82          39 S L76 AND L80,L81
L83          19 S L82 AND PY<=1995
L84          19 S L83 NOT L77
L85          12 S L84 AND INFUS?
L86          14 S L79,L85
L87           7 S L84 NOT L86
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FILE 'EMBASE' ENTERED AT 13:43:41 ON 10 APR 2000

=> d all tot l86

L86 ANSWER 1 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

AN 95159725 EMBASE

DN 1995159725

TI Pharmacokinetic, insulinotropic, and glucagonostatic properties of GLP-1 [7-36 amide] after subcutaneons injection in healthy volunteers. Dose-response-relationships.

AU Ritzel R.; Orskov C.; Holst J.J.; **Nauck M.A.**

CS Department of Medicine, Ruhr-University Bochum, Knappschafts-Krankenhaus, In der Schornau 23-25,D-44892 Bochum, Germany

SO Diabetologia, (1995) 38/6 (720-725).
ISSN: 0012-186X CODEN: DBTGAJ

CY Germany

DT Journal; Article

FS 003 Endocrinology
006 Internal Medicine
037 Drug Literature Index

LA English

SL English

AB Intravenous **infusions** of **glucagon-like peptide 1** (GLP-1) [7-36 amide] are **glucose**-dependently insulinotropic and glucagonostatic and normalize plasma **glucose** concentrations in non-insulin-dependent diabetic patients. It was the aim of this study to investigate whether subcutaneous GLP-1 [7-36 amide] also has an influence on insulin and glucagon secretion, and which doses are required for significant effects. Therefore, eight healthy volunteers (24 .+-. 2 years, body mass index [BMI] 21.9 .+-. 2.3 kg/m2) were studied in the fasting state on five occasions in randomized order. Placebo (0.9% NaCl with 1% human serum albumin) or GLP-1 1:7-36 amide] in

doses of 0.15, 0.5, 1.5 or 4.5 nmol/kg body weight (volume 1 ml or, at the highest dose, 2 ml) was administered subcutaneously. An intravenous **glucose** bolus (0.33 g/kg body weight) was injected 30 min later. Blood was drawn for the measurement of **glucose**, insulin, C-peptide, GLP-1 [7-36 amide], and glucagon using specific radioimmunoaasays. There were dose-related increments in GLP-1 [7-36 amide] concentrations ($p < 0.0001$). However, basal values were reached again after 90-120 min. Before **glucose** administration, insulin ($p < 0.0001$) and C-peptide ($p < 0.0004$) increased, whereas glucagon ($p = 0.0018$) and **glucose** $p < 0.0001$) decreased in a dose-dependent manner. After **glucose** stimulation, integrated increments in insulin ($p = 0.0007$) and C-peptide ($p = 0.02$) were augmented and k(G)-values increased $p < 0.0001$) in a dose-related fashion. The extent of reactive hypoglycaemia was related to the GLP-1 [7-36 amide] dose. With the highest GLP-1 [7-36 amide] dose, at the time of peak plasma concentrations, most volunteers felt unwell, and nausea and vomiting were observed in four subjects. In conclusion, subcutaneous GLP-1 [7-36 amide] is also able to stimulate insulin and inhibit glucagon secretion, thereby altering **glucose** assimilation. However, with unmodified GLP-1 [7-36 amide], the duration of action is short, and with high doses side effects are common.

CT Medical Descriptors:
*glucagon release
*insulin release
adult
article
clinical protocol
clinical trial
drug administration
drug effect
female
human
human experiment
intravenous drug administration
male
normal human
priority journal
radioimmunoassay
subcutaneous drug administration
Drug Descriptors:
***glucagon like peptide 1 [7-36] amide: PD, pharmacology**
***glucagon like peptide 1 [7-36] amide: DO, drug dose**
***glucagon like peptide 1 [7-36] amide: AD, drug administration**
c peptide: EC, endogenous compound
glucagon: EC, endogenous compound
glucose: EC, endogenous compound
insulin: EC, endogenous compound

RN (**glucagon like peptide 1** [7-36] amide) 119637-73-9; (c peptide) 59112-80-0; (glucagon) 11140-85-5, 62340-29-8, 9007-92-5; (**glucose**) **50-99-7**, 84778-64-3; (insulin) 9004-10-8

CO Saxon (Germany)

L86 ANSWER 2 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 95159414 EMBASE
DN 1995159414
TI Physiological augmentation of amino acid-induced insulin secretion by **GIP** and GLP-I but not by CCK-8.
AU Fieseler P.; Bridenbaugh S.; Nustede R.; Martell J.; Orskov C.; Holst J.J.; **Nauck M.A.**
CS Dept. of Medicine, Knappschafts-Krankenhaus, Ruhr University Bochum, In der Schornau 23-25,44892 Bochum, Germany
SO American Journal of Physiology - Endocrinology and Metabolism, (1995) 268/5 31-5 (E949-E955).
ISSN: 0193-1849 CODEN: AJPMD
CY United States

DT Journal; Article
FS 002 Physiology
003 Endocrinology
LA English
SL English
AB It was the aim of this study to test insulinotropic actions of cholecystokinin octapeptide (CCK-8), **gastric inhibitory polypeptide** (**GIP**), and **glucagon-like peptide I** (GLP-I)-(7-36) amide at basal **glucose** but physiologically elevated amino acid concentrations. Therefore, in nine fasting healthy volunteers, an amino acid mixture was **infused** intravenously (12.6 g/h over 120 min). On separate occasions, from 30 to 120 min, placebo (0.9% NaCl-1% human serum albumin), synthetic sulfated CCK-8 (0.5 pmol .cntdot. kg-1 .cntdot. min-1), human **GIP** (1 pmol .cntdot. kg-1 .cntdot. min-1), or GLP-I-(7-36) amide (0.3 pmol .cntdot. kg-1 .cntdot. min-1) was **infused** intravenously to mimic physiological increments after a meal. The amino acid **infusion** lead to a small increment in plasma **glucose** from 4.8 .+-. 0.2 to 5.0 .+-. 0.2 mmol/l and significantly elevated insulin and C-peptide concentrations. **GIP** and GLP-I- (7-36) amide further stimulated insulin (1.8-fold, P = 0.0001 and 0.004, respectively) and C-peptide (1.3-fold, P = 0.0003 and 0.013, respectively), with a subsequent slight reduction in plasma **glucose** (P < 0.0001). Insulin and C-peptide then decreased again in parallel. CCK-8 was without effect on insulin and C-peptide levels. In conclusion, **GIP** and GLP-I-(7-36) amide are not only able to interact with elevated plasma **glucose** but are insulinotropic also with physiologically raised amino acid concentrations. Such an interaction could play a role after the ingestion of mixed meals. Cholecystokinin, on the other hand, is not a physiological incretin also under these conditions.
CT Medical Descriptors:
*insulin release
adult
amino acid blood level
article
glucose blood level
glucose metabolism
hormonal regulation
human
human experiment
insulin like activity
male
normal human
priority journal
Drug Descriptors:
*cholecystokinin octapeptide
***gastric inhibitory polypeptide**
***glucagon like peptide 1**
*insulin: EC, endogenous compound
glucose: EC, endogenous compound
RN (cholecystokinin octapeptide) 25126-32-3; (**gastric inhibitory polypeptide**) **59392-49-3**; (**glucagon like peptide 1**) **89750-14-1**; (insulin) 9004-10-8; (**glucose**) **50-99-7**, 84778-64-3

L86 ANSWER 3 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 95131371 EMBASE
DN 1995131371
TI Insulinotropic actions of intravenous **glucagon-like peptide-1** (GLP-1) [7-36 amide] in the fasting state in healthy subjects.
AU Qualmann C.; **Nauck M.A.**; Holst J.J.; Orskov C.; Creutzfeldt W.
CS Medizinische Universitatsklinik, Ruhr-Universitat Bochum, Knappschaftskrankenhaus, In der Schornau 23-25,D-44892 Bochum, Germany
SO Acta Diabetologica, (1995) 32/1 (13-16).

ISSN: 0940-5429 CODEN: ACDAEZ
CY Germany
DT Journal; Article
FS 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB GLP-1 (7-36 amide) stimulates insulin and suppresses glucagon secretion in normal subjects and may, in pharmacological doses, normalize hyperglycaemia in type 2 diabetic patients. It is not known whether such pharmacological doses can actually lower blood **glucose** to hypoglycaemic levels. Therefore, in seven normal fasting subjects, GLP-1 (7-36 amide) was **infused** intravenously at 0.3, 0.9 and 2.7 pmol/kg per min for 30 min each. The plasma concentration of GLP-1 (7-36 amide) increased dose-dependently, but insulin secretion (insulin, C-peptide) was stimulated only marginally. Glucagon was slightly suppressed, and plasma **glucose** was reduced, but not into the hypoglycaemic range. In conclusion, when plasma **glucose** concentrations are in the normal fasting range, GLP-1 (7-36 amide) is not able to stimulate insulin secretion to a degree that causes hypoglycaemia. This should limit the risk of hypoglycaemic responses when GLP-1 (7-36 amide) is administered in pharmacological doses to reduce hyperglycaemia in type 2 diabetic patients.
CT Medical Descriptors:
*insulin release
adult
article
clinical trial
controlled study
diet restriction
dose response
drug effect
glucagon release
glucose blood level
human
human experiment
hyperglycemia
hypoglycemia
intravenous drug administration
male
non insulin dependent diabetes mellitus
normal human
priority journal
Drug Descriptors:
***glucagon like peptide 1 [7-36] amide: CT, clinical trial**
***glucagon like peptide 1 [7-36] amide: PD, pharmacology**
c peptide: EC, endogenous compound
glucagon: EC, endogenous compound
glucose: EC, endogenous compound
insulin: EC, endogenous compound
RN (**glucagon like peptide 1** [7-36] amide) 119637-73-9; (c peptide) 59112-80-0; (glucagon) 11140-85-5, 62340-29-8, 9007-92-5; (**glucose**) **50-99-7**, 84778-64-3; (insulin) 9004-10-8
CO Saxon (Germany)

L86 ANSWER 4 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 93286381 EMBASE
DN 1993286381
TI Preserved incretin effect in type 1 diabetic patients with end-stage nephropathy treated by combined heterotopic pancreas and kidney transplantation.
AU **Nauck M.A.**; Busing M.; Orskov C.; Siegel E.G.; Talartschik J.;

Baartz A.; Baartz T.; Hopt U.T.; Becker H.-D.; Creutzfeldt W.
CS Div. of Gastroenterol./Endocrinology, Department of Medicine, Georg August University, Robert-Koch-Strasse 40,W-3400 Gottingen, Germany
SO Acta Diabetologica, (1993) 30/1 (39-45).
ISSN: 0940-5429 CODEN: ACDAEZ
CY Germany
DT Journal; Article
FS 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
LA English
SL English
AB Insulin secretion is stimulated better by oral than by intravenous **glucose** (incretin effect). The contribution of the autonomic nervous system to the incretin effect after oral **glucose** in humans is unclear. We therefore examined nine type 1 diabetic (insulin-dependent) patients with end-stage nephropathy, studied after combined heterotopic pancreas and kidney transplantation, and 7 non-diabetic kidney recipients (matched for creatinine clearance and immunosuppressive medication). The release of **gastric inhibitory polypeptide** (**GIP**) and **glucagon-like peptide 1** (GLP-1) immunoreactivity and B cell secretory responses (IR insulin and C-peptide) to oral (50 g) and 'isoglycaemic' intravenous **glucose** (identical glycaemic profile)were measured by radioimmunoassay. The difference in B cell responses between the two tests represents the contribution of the enteroinsular axis to the response after oral **glucose** (incretin effect). Insulin responses after the oral **glucose** challenge were similar in the two patient groups despite systemic venous drainage of the pancreas graft in the pancreas-kidney-transplanted group. In both groups **GIP** and GLP-1 increased after oral but not after intravenous **glucose**, and B cell secretory responses were significantly smaller (by 55.2 .+-. 7.7% and 46.5 .+-. 12.5%, respectively) with 'isoglycaemic' intravenous **glucose infusions**. The lack of reduction in the incretin effect in pancreas-kidney-transplanted patients, whose functioning pancreas is denervated, indicates a lesser role for the nervous system and a more important contribution of circulating incretin hormones in mediating the enteroinsular axis in man.
CT Medical Descriptors:
*diabetic nephropathy: SU, surgery
*insulin dependent diabetes mellitus
*kidney transplantation
*pancreas transplantation
adult
article
clinical article
controlled study
female
human
male
Drug Descriptors:
***gastric inhibitory polypeptide: EC, endogenous compound**
***glucagon like peptide 1: EC, endogenous compound**
***glucose**
*insulin: EC, endogenous compound
RN (**gastric inhibitory polypeptide**) **59392-49-3**; (**glucagon like peptide 1**) **89750-14-1**; (**glucose**) **50-99-7**, 84778-64-3; (insulin) 9004-10-8

L86 ANSWER 5 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 93218656 EMBASE
DN 1993218656
TI Normalization of fasting hyperglycaemia by exogenous **glucagon-like peptide 1** (7-36 amide) in Type 2 (non-insulin-dependent) diabetic patients.

AU **Nauck M.A.**; Kleine N.; Orskov C.; Holst J.J.; Willms B.; Creutzfeldt W.
CS Medizinische Klinik, Ruhr-Universitat, Knappschafts-Krankenhaus, In der Schornau 23-25,D-44892 Bochum, Germany
SO Diabetologia, (1993) 36/8 (741-744).
ISSN: 0012-186X CODEN: DBTGAJ
CY Germany
DT Journal; Article
FS 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB **Glucagon-like peptide 1** (GLP-1) (7-36 amide) is a physiological incretin hormone that is released after nutrient intake from the lower gut and stimulates insulin secretion at elevated plasma **glucose** concentrations. Type 2 (non-insulin-dependent) diabetic patients GLP-1 (7-36 amide) retains much of its insulinotropic action. However, it is not known whether the magnitude of this response is sufficient to normalize plasma **glucose** in Type 2 diabetic patients with poor metabolic control. Therefore, in 10 Type 2 diabetic patients with unsatisfactory metabolic control (HbA(1c) 11.6 .+-. 1.7%) on diet and sulphonylurea therapy (in some patients supplemented by metformin or acarbose), 1.2 pmol x 1-1 x min-1 GLP-1 (7-36 amide) or placebo was **infused** intravenously in the fasting state (plasma **glucose** 13.1 .+-. 0.6 mmol/l). In all patients, insulin (by 17.4 .+-. 4.7 nmol x 1-1 x min; p = 0.0157) and C-peptide (by 228.0 .+-. 39.1 nmol x 1-1 x min; p = 0.0019) increased significantly over basal levels, glucagon was reduced (by -1418 .+-. 308 pmol x 1-1 x min) and plasma **glucose** reached normal fasting concentrations (4.9 .+-. 0.3 mmol/l) within 4 h of GLP-1 (7-36 amide) administration, but not with placebo. When normal fasting plasma **glucose** concentrations were reached insulin returned towards basal levels and plasma **glucose** concentrations remained stable despite the ongoing **infusion** of GLP-1 (7-36 amide). Therefore, exogenous GLP-1 (7-36 amide) is an effective means of normalizing fasting **glucose** concentrations in poorly-controlled Type 2 diabetic patients. The **glucose**-dependence of insulinotropic actions of GLP-1 (7-36 amide) appears to be retained in such patients.
CT Medical Descriptors:
*caloric restriction
*hyperglycemia: PC, prevention
*non insulin dependent diabetes mellitus: DT, drug therapy
adult
article
clinical article
controlled study
female
human
intravenous drug administration
male
priority journal
Drug Descriptors:
*acarbose: DT, drug therapy
*c peptide: EC, endogenous compound
*glucagon: EC, endogenous compound
***glucagon like peptide: PD, pharmacology**
***glucose: EC, endogenous compound**
*insulin: EC, endogenous compound
*metformin: DT, drug therapy
*placebo
*sulfonylurea derivative: DT, drug therapy
RN (acarbose) 56180-94-0; (c peptide) 59112-80-0; (glucagon) 11140-85-5, 62340-29-8, 9007-92-5; (**glucagon like peptide**) 82905-30-4; (**glucose**) **50-99-7**, 84778-64-3; (insulin)

9004-10-8; (metformin) 1115-70-4, 657-24-9
CO Saxon (Germany)

L86 ANSWER 6 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 93110837 EMBASE
DN 1993110837
TI Additive insulinotropic effects of exogenous synthetic human **gastric inhibitory polypeptide** and **glucagon-like peptide-1**-(7-36) amide **infused** at near-physiological insulinotropic hormone and **glucose** concentrations.
AU **Nauck M.A.**; Bartels E.; Orskov C.; Ebert R.; Creutzfeldt W.
CS Gastroenterology/Endocrinology Div., Department of Internal Medicine, Georg August University, Robert Koch Strasse 40,D 3400 Gottingen, Germany
SO Journal of Clinical Endocrinology and Metabolism, (1993) 76/4 (912-917). ISSN: 0021-972X CODEN: JCEMAZ
CY United States
DT Journal; Article
FS 003 Endocrinology
LA English
SL English
AB **Gastric inhibitory polypeptide** (**GIP**) and **glucagon-like peptide-1**-(7-36) amide (GLP-1) are **glucose**-dependent insulinotropic gut hormones that may explain the greater insulin secretory response with oral compared to iv **glucose** (incretin effect). To study their individual and combined contributions, in eight healthy volunteers, on separate occasions, synthetic human **GIP** (1 pmol/kg .cntdot. min) and/or GLP-1 (0.3 pmol/kg .cntdot. min) or placebo were **infused** iv (-30 to 120 min), while at 0 min, a **glucose infusion** 'isoglycemic' to the profile after an oral **glucose** load of 50 g/400 mL was started. After the administration of 50 g oral **glucose**, immunoreactive **GIP** rose several-fold to 337 .+-. 43 pmol/L, while there was only a transient (10- 30 min) and moderate increment in immunoreactive GLP-1 (from basal, 25-30, to 41 .+-. 4 pmol/L). Isoglycemic iv **glucose infusions** led to smaller B-cell responses (estimated incretin effect, 41 .+-. 5%). With single **infusions** of **GIP** or GLP-1 (circulating concentrations, 464 .+-. 73 and 54 .+-. 3 pmol/L, respectively), B-cell responses were significantly augmented compared to iv **glucose** alone and were no longer significantly different from those after oral **glucose**. The combination of **GIP** and GLP-1 led to B-cell responses that were significantly higher than those with either hormone alone (additive mode of cooperation). Plasma **GIP** concentrations were similar after endogenous secretion (oral **glucose**) and iv **infusion**, while exogenously administered GLP- 1 led to plasma levels that were maintained at an elevated level for a longer period during exogenous **infusion** than after stimulation by oral **glucose**. When, in seven volunteers, a lower dose (0.15 pmol/kg .cntdot. min) of GLP-1 was **infused** during isoglycemic **glucose infusion** experiments only for the duration of elevated plasma levels in the oral **glucose** challenges (0-30 min), a significant, but transient, increment in insulin and concentrations was observed, which was equivalent to 26 .+-. estimated incretin effect. Therefore, in conclusion, circula **GIP** seems to make a major contribution to the incretin effec after oral **glucose**, and GLP-1 appears to mediate a smaller proportion. **GIP** and GLP-1 can interact in an additive manne normal man.
CT Medical Descriptors:
*insulin like activity
***oral glucose tolerance test**
article
hormone release
human
human experiment

intravenous glucose tolerance test
male
normal human
pancreas islet beta cell
priority journal
Drug Descriptors:
*c peptide: EC, endogenous compound
***gastric inhibitory polypeptide**
***glucagon like peptide 1 [7-36] amide**
***glucose: EC, endogenous compound**
*insulin: EC, endogenous compound
RN (c peptide) 59112-80-0; (**gastric inhibitory polypeptide**) **59392-49-3**; (**glucagon like peptide 1** [7-36] amide) 119637-73-9; (**glucose**) **50-99-7**, 84778-64-3; (insulin) 9004-10-8

L86 ANSWER 7 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 93040953 EMBASE
DN 1993040953
TI Role of endogenously released cholecystokinin in determining postprandial insulin levels in man: Effects of loxiglumide, a specific cholecystokinin receptor antagonist.
AU Baum F.; **Nauck M.A.**; Ebert R.; Cantor P.; Hoffmann G.; Choudhury A.R.; Schmidt W.E.; Creutzfeldt W.
CS Division of Gastroenterology, Department of Medicine, Georg August University, Robert-Koch-Strasse 40,D-W-3400 Gottingen, Germany
SO Digestion, (1992) 53/3-4 (189-199).
ISSN: 0012-2823 CODEN: DIGEBW
CY Switzerland
DT Journal; Article
FS 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LA English
SL English
AB To estimate the contribution of postprandial cholecystokinin (CCK) responses to circulating insulin concentrations and insulin secretion, a specific CCK receptor antagonist (loxiglumide; 10 mg/kg body weight/h) or saline were **infused** intravenously in normal volunteers, beginning 90 min before insulin secretion was stimulated on separate occasions by the intraduodenal administrations of **glucose**, **glucose** and protein, and **glucose** plus protein with the admixture of pancreatin. The release of CCK (radioimmunoassay) was stimulated by the protein component of the nutrients from basal 2.4 .+-. 0.4 to 8.0 .+-. 1.2 pmol/l. CCK plasma levels were significantly higher with loxiglumide ($p<0.05$). **Glucose-dependent insulinotropic polypeptide** (**GIP**) was also released by all nutrient mixtures. Loxiglumide significantly inhibited the amount of bilirubin and pancreatic enzymes recovered from duodenal aspirates. In contrast, in none of the experiments, C-peptide increments and hence insulin secretion rates were altered by loxiglumide. With **glucose** and protein as intraduodenal stimulus (no pancreatin added), the plasma amino acids rose significantly less (by approximately 50% of the control experiment) and the increment in insulin (but not C-peptide) concentrations was significantly reduced by loxiglumide. This is most likely explained by a change in insulin metabolic clearance. This effect cannot be a primary action of CCK because there was no similar effect of loxiglumide with the same intraduodenal stimulus plus added pancreatin. Pancreatic enzymes reduced maldigestion secondary to loxiglumide effects on pancreatic exocrine secretion: The increment in circulating amino acid concentrations was similar with and without loxiglumide. In conclusion, CCK does not alter insulin secretion and, therefore, is not an incretin hormone in man. Blocking CCK actions on the exocrine pancreas by loxiglumide, however, can secondarily cause reductions in postprandial insulin profiles by altering insulin clearance.

These changes are possibly related to reductions in circulating amino acid concentrations.

CT Medical Descriptors:
*insulin release
*postprandial state
adult
amino acid blood level
article
aspiration
cholecystokinin blood level
controlled study
drug blood level
drug effect
duodenum
human
human experiment
insulin blood level
insulin metabolism
intravenous drug administration
male
normal human
pancreas function
priority journal
volunteer
Drug Descriptors:
*cholecystokinin receptor
*cholecystokinin: EC, endogenous compound
*cholecystokinin receptor blocking agent: CR, drug concentration
*cholecystokinin receptor blocking agent: PD, pharmacology
*cholecystokinin receptor blocking agent: DO, drug dose
*insulin: EC, endogenous compound
*loxiglumide: CR, drug concentration
*loxiglumide: DO, drug dose
*loxiglumide: PD, pharmacology
amino acid: EC, endogenous compound
bilirubin: EC, endogenous compound
c peptide: EC, endogenous compound
glucose
pancreas polypeptide: EC, endogenous compound
pancreatin
protein

RN (cholecystokinin) 9011-97-6, 93443-27-7; (insulin) 9004-10-8; (loxiglumide) 107097-80-3; (amino acid) 65072-01-7; (bilirubin) 18422-02-1, 635-65-4; (c peptide) 59112-80-0; (**glucose**) **50-99-7**, 84778-64-3; (pancreas polypeptide) 59763-91-6; (pancreatin) 8049-47-6; (protein) 67254-75-5

CN (1) Cr 1505

CO (1) Rotta (Italy)

L86 ANSWER 8 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

AN 93037285 EMBASE

DN 1993037285

TI Preserved incretin activity of **glucagon-like peptide 1** [7-36 amide] but not of synthetic human **gastric inhibitory polypeptide** in patients with type- 2 diabetes mellitus.

AU **Nauck M.A.**; Heimesaat M.M.; Orskov C.; Holst J.J.; Ebert R.; Creutzfeldt W.

CS Gastroenterology/Endocrinology Div., Department of Internal Medicine, Georg-August-Universitat, Robert-Koch-Strasse 40,D-3400 Gottingen, Germany

SO Journal of Clinical Investigation, (1993) 91/1 (301-307). ISSN: 0021-9738 CODEN: JCINAO

CY United States

DT Journal; Article

FS 003 Endocrinology

LA English

SL English
AB In type-2 diabetes, the overall incretin effect is reduced. The present investigation was designed to compare insulinotropic actions of exogenous incretin hormones (**gastric inhibitory peptide** [**GIP**] and **glucagon-like peptide 1** [GPL-1] [7-36 amide]) in nine type-2 diabetic patients (fasting plasma **glucose** 7.8 mmol/liter; hemoglobin A(1c) 6.3.+-.0.6%) and in nine age- and weight-matched normal subjects. Synthetic human **GIP** (0.8 and 2.4 pmol/kg .cntdot. min over 1 h each), GLP-1 [7-36 amide] (0.4 and 1.2 pmol/kg .cntdot. min over 1 h each), and placebo were administered under hyperglycemic clamp conditions (8.75 mmol/liter) in separate experiments. Plasma **GIP** and GLP-1 [7-36 amide] concentrations (radioimmunoassay) were comparable to those after oral **glucose** with the low, and clearly supraphysiological with the high **infusion** rates. Both **GIP** and GLP-1 [7-36 amide] dose-dependently augmented insulin secretion (insulin, C-peptide) in both groups ($P < 0.05$). With **GIP**, the maximum effect in type-2 diabetic patients was significantly lower (by 54%; $P < 0.05$) than in normal subjects. With GLP-1 [7-36 amide] type-2 diabetic patients reached 71% of the increments in C-peptide of normal subjects (difference not significant). Glucagon was lowered during hyperglycemic clamps in normal subjects, but not in type-2 diabetic patients, and further by GLP-1 [7-36 amide] in both groups ($P < 0.05$), but not by **GIP**. In conclusion, in mild type-2 diabetes, GLP-1 [7-36 amide], in contrast to **GIP**, retains much of its insulinotropic activity. It also lowers glucagon concentrations.
CT Medical Descriptors:
*non insulin dependent diabetes mellitus
adult
aged
article
clinical article
controlled study
female
glucose clamp technique
human
insulin like activity
insulin release
intravenous glucose tolerance test
male
oral glucose tolerance test
priority journal
Drug Descriptors:
*c peptide: EC, endogenous compound
***gastric inhibitory polypeptide: EC, endogenous compound**
*glucagon: EC, endogenous compound
***glucagon like peptide 1 [7-36] amide: EC, endogenous compound**
***glucose: EC, endogenous compound**
*insulin: EC, endogenous compound
hemoglobin a1c: EC, endogenous compound
RN (c peptide) 59112-80-0; (**gastric inhibitory polypeptide**) **59392-49-3**; (glucagon) 11140-85-5, 62340-29-8, 9007-92-5; (**glucagon like peptide 1** [7-36] amide) 119637-73-9; (**glucose**) **50-99-7**, 84778-64-3; (insulin) 9004-10-8; (hemoglobin a1c) 62572-11-6

L86 ANSWER 9 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 92350254 EMBASE
DN 1992350254
TI Lack of effect of synthetic human **gastric inhibitory polypeptide** and **glucagon-like peptide 1** [7-36 amide] **infused** at near-physiological concentrations on pentagastrin-stimulated gastric acid secretion in normal human subjects.
AU **Nauck M.A.**; Bartels E.; Orskov C.; Ebert R.; Creutzfeldt W.
CS Div Gastroenterology/Endocrinology, Department of Internal Medicine,

Georg-August-University, Robert-Koch-Strasse 40,D-W-3400 Gottingen, Germany
SO Digestion, (1992) 52/3-4 (214-221).
ISSN: 0012-2823 CODEN: DIGEBW
CY Switzerland
DT Journal; Article
FS 002 Physiology
037 Drug Literature Index
048 Gastroenterology
LA English
SL English
AB **Gastric inhibitory polypeptide** (**GIP**) and **glucagon-like peptide 1** [7-36 amide] (GLP-1) are **glucose**-dependent insulinotropic gut hormones. Under experimental conditions, both have been shown to reduce stimulated gastric acid secretion. To study their individual and combined effects on pentagastrin-stimulated (0.1 .mu.g/kg/h from - 90 to 120 min) gastric volume, acid and chloride output, on separate occasions, synthetic human **GIP** (1 pmol/kg/min) and/or GLP-1 [7-36 amide] (0.3 pmol/kg/min) or placebo (0.9% NaCl with 1% albumin) were **infused** intravenously (from - 30 to 120 min) in 9 healthy volunteers. At 0 min, a **glucose infusion** was started that mimicked the glycemic profile after an oral **glucose** load of 50 g/400 ml and allowed for the **glucose**-dependent insulinotropic action of **GIP** and GLP-1 [7-36 amide]. Pentagastrin stimulated acid output significantly, but neither **GIP** nor GLP-1 [7-36 amide] either alone or in combination, reduced pentagastrin-stimulated gastric acid secretion. The circulating concentrations of **GIP** and GLP-1 [7-36 amide] obtained at steady state during exogenous administration of synthetic peptides were similar to or higher than those reached after oral **glucose** (endogenous secretion). In conclusion, (penta)gastrin-stimulated gastric acid secretion is not inhibited by physiological circulating concentrations of **GIP** or GLP-1 [7-36 amide]. Therefore, the insulinotropic action of these intestinal hormones is physiologically more important than their possible role as enterogastrone.
CT Medical Descriptors:
*drug effect
*stomach acid secretion
adult
article
clinical article
glucose infusion
human
insulin release
intravenous drug administration
male
normal human
oral glucose tolerance test
priority journal
stomach acid
stomach volume
Drug Descriptors:
***gastric inhibitory polypeptide**
***glucagon like peptide 1 [7-36] amide**
*pentagastrin
chloride: EC, endogenous compound
insulin: EC, endogenous compound
RN (**gastric inhibitory polypeptide**) **59392-49-3**; (**glucagon like peptide 1** [7-36] amide) 119637-73-9; (pentagastrin) 5534-95-2; (chloride) 16887-00-6; (insulin) 9004-10-8
CO Bissendorf (Germany)

AN 90002403 EMBASE

DN 1990002403
TI Suppression of insulin receptor binding by **prolonged** enteral or **parenteral** nutrient infusion in the rat: Role of **gastric inhibitory polypeptide**.
AU Baer A.R.; Dupre J.
CS Department of Physiology, University of Western Ontario, London, Ont., Canada
SO Canadian Journal of Physiology and Pharmacology, (1989) 67/9 (1105-1109).
ISSN: 0008-4212 CODEN: CJPPA3
CY Canada
DT Journal; Article
FS 002 Physiology
003 Endocrinology
037 Drug Literature Index
LA English
SL French; English
AB In the rat, prolonged enteral or **parenteral** alimentation with a high-carbohydrate diet results in hyperinsulinemia, which is substantially greater with the **parenteral** route. Supplementing the **parenteral** infusate with porcine **gastric inhibitory polypeptide** (**GIP**) to approximate plasma immunoreactive **GIP** levels achieved with enteral feeding further increases steady-state plasma insulin and **glucose** concentrations, suggesting insulin resistance. We examined the effects of sustained hyperinsulinemia elicited by continuous nutrient infusion on insulin binding to isolated rat adipocytes and the modification of this response by **GIP**. Compared with a baseline group, both enterally and **parenterally** alimented groups showed decreased insulin receptor binding affinity. However, despite substantially different steady-state plasma insulin levels, insulin binding was similar with either infusion route. Factors other than plasma insulin concentration alone therefore contribute to insulin receptor down-regulation during prolonged enteral alimentation. Supplementing the **parenteral** infusate with exogenous **GIP** resulted in a further reduction in insulin receptor affinity. Thus, adaptation to continuous nutrient infusion is characterized by insulin receptor down-regulation regardless of the route of nutrient delivery. An additional suppression of insulin receptor binding may in part be responsible for the insulin resistance elicited by prolonged exogenous **GIP** administration.
CT Medical Descriptors:
*adipocyte
***glucose blood level**
*hyperinsulinemia
*insulin resistance
***parenteral nutrition**
cell culture
rat
controlled study
animal experiment
animal cell
nonhuman
male
article
priority journal
Drug Descriptors:
*insulin receptor
radioisotope
***gastric inhibitory polypeptide: PD, pharmacology**
*insulin: TO, drug toxicity
*insulin: DO, drug dose
RN (**gastric inhibitory polypeptide**)
59392-49-3; (insulin) 9004-10-8

L86 ANSWER 11 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 89221284 EMBASE
DN 1989221284

TI Insulinotropic properties of synthetic human **gastric inhibitory polypeptide** in man: Interactions with **glucose**, phenylalanine, and cholecystokinin-8.

AU **Nauck** M.; Schmidt W.E.; Ebert R.; Strietzel J.; Cantor P.; Hoffmann G.; Creutzfeldt W.

CS Division of Gastroenterology and Endocrinology, Department of Medicine, Georg-August-University Gottingen, D-3400 Gottingen, Germany

SO Journal of Clinical Endocrinology and Metabolism, (1989) 69/3 (654-662). ISSN: 0021-972X CODEN: JCEMAZ

CY United States

DT Journal

FS 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index

LA English

SL English

AB The quantitative contribution of **glucose-dependent insulinotropic polypeptide [gastric inhibitory polypeptide (GIP)]** to the incretin effect after oral **glucose** (augmentation of insulin secretion over the degree that is explained by the glycemic rise) is not known. Therefore, hyperglycemic clamp experiments (8 mmol/L, corresponding to postprandial **glucose** concentrations) were performed in healthy volunteers and synthetic human **GIP** was **infused** for 60 min at a rate (.apprx.1.3 pmol/kg.cntdot.min) that results in plasma **GIP** concentrations similar to those occurring after oral **glucose** loads of 75 g. The MCR for exogenous **GIP** was .apprx.6 mL/kg.cntdot.min; the decay after ceasing **infusion** was exponential with a t(1/2) of about 18 min, and the resulting volume of distribution was about 140 mL/kg. At euglycemic (basal) plasma **glucose** concentrations (5.0 mmol/L) similar values were found. Insulin secretion was stimulated by hyperglycemia alone, but was greatly (2.3-fold based on C-peptide) potentiated by **GIP infusions** (P .ltoreq. 0.001 for integrated incremental values). When integrated incremental responses over 120 min of **GIP**, immunoreactive insulin, and immunoreactive C-peptide were compared after oral **glucose** and during **GIP infusions**, no significant differences were found. Peak **glucose** concentrations after oral **glucose** (7.6 .+-. 0.6 mmol/L) were similar to mean plasma **glucose** values during clamp experiments (8.2 .+-. 0.1 mmol/L; P = 0.124). However, mean **glucose** concentrations after oral **glucose** were lower (6.0 .+-. 0.3 mmol/L; P = 0.0004). Additional **infusion** of sulfated cholecystokinin-8 (25 pmol/kg.cntdot.h) or the amino acid phenylalanine (1.7 .mu.mol/kg.cntdot.min) did not further stimulate insulin secretion and had no influence on the pharmacokinetics of exogenous **GIP**. It is concluded that human synthetic **GIP** is insulinotropic in man and that this activity may well explain a substantial part of the incretin effect after oral **glucose**. There is no interaction with cholecystokinin or phenylalanine in concentrations found after mixed meals.

CT Medical Descriptors:
*incretin
*insulin release
adult
human experiment
human
normal human
male
female
priority journal
Drug Descriptors:
c peptide

*cholecystokinin octapeptide: IT, drug interaction
***gastric inhibitory polypeptide: PD, pharmacology**
***gastric inhibitory polypeptide: IT, drug interaction**
***gastric inhibitory polypeptide: PK, pharmacokinetics**
***glucose: IT, drug interaction**
*phenylalanine: IT, drug interaction
RN (c peptide) 59112-80-0; (cholecystokinin octapeptide) 25126-32-3; (**gastric inhibitory polypeptide**) **59392-49-3**; (**glucose**) **50-99-7**, 84778-64-3; (phenylalanine) 3617-44-5, 63-91-2
CO Peninsula (United Kingdom); Braun melsungen

L86 ANSWER 12 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 88175636 EMBASE
DN 1988175636
TI Lack of insulinotropic effect of endogenous and exogenous cholecystokinin in man.
AU Reimers J.; **Nauck M.**; Creutzfeldt W.; Strietzel J.; Cantor P.; Hoffmann G.
CS Division of Gastroenterology and Endocrinology, Department of Medicine, Georg August University, D-3400 Gottingen, Germany
SO Diabetologia, (1988) 31/5 (271-280).
ISSN: 0012-186X CODEN: DBTGAJ
CY Germany
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
006 Internal Medicine
048 Gastroenterology
LA English
SL English
AB Intraduodenal phenylalanine administration (333 mg/min over 60 min) released endogenous cholecystokinin in healthy young subjects as demonstrated radioimmunologically and by intraduodenal bilirubin and pancreatic enzyme output. Concomitantly, there was only a small increase over basal in circulating immunoreactive-insulin and immunoreactive-C-peptide concentrations. In healthy volunteers intraduodenal **infusions** of saline (10 ml/min), **glucose** (333 mg/min) or phenylalanine (333 mg/min) were performed for 60 min when plasma **glucose** was clamped at approximately 8 mmol/l. Phenylalanine enhanced immunoreactive-insulin and immunoreactive-C-peptide responses three-fold more than did the same amount of **glucose**. Immuno-reactive **gastric inhibitory polypeptide** responses were small and not different after **glucose** and phenylalanine administration. Immunoreactive cholecystokinin was significantly stimulated to 9.4 .+-. 1.4 pmol/l only by intraduodenal phenylalanine. Plasma phenylalanine concentrations increased into the supraphysiological range (approximately 1.5 mmol/l). Intravenous **infusions** of phenylalanine achieving plasma concentrations of 1.2 mmol/stimulated insulin secretion at elevated plasma **glucose** concentrations (approximately 8 mmol/l clamp experiments), but had no effect at basal plasma **glucose** concentrations. A small increase in cholecystokinin also was observed. Intravenous **infusions** of synthetic sulphated cholecystokinin-8 leading to plasma concentrations in the upper postprandial range (8-12 pmol/l) did not augment the immunoreactive-insulin or immunoreactive-C-peptide levels during hyperglycaemic clamp experiments, in the absence or presence of elevated plasma phenylalanine concentrations. It is concluded that the augmentation of the **glucose**-induced insulin release by intraduodenal administration of phenylalanine cannot be related to cholecystokinin release, but rather is explained by the combined effects of elevated **glucose** and phenylalanine concentrations. In man, cholecystokinin does not augment insulin secretion caused by moderate hyperglycaemia, elevations of phenylalanine concentrations, or combinations thereof.
CT Medical Descriptors:
***glucose blood level**

*hyperglycemia
*insulin release
duodenum
human
incretin effect
priority journal
normal human
clinical article
human experiment
intravenous drug administration
Drug Descriptors:
*c peptide
***gastric inhibitory polypeptide**
*phenylalanine
bilirubin
pancreas enzyme
*cholecystokinin octapeptide

RN (c peptide) 59112-80-0; (**gastric inhibitory polypeptide**) **59392-49-3**; (phenylalanine) 3617-44-5, 63-91-2; (bilirubin) 18422-02-1, 635-65-4; (cholecystokinin octapeptide) 25126-32-3

CO Bachem (Switzerland)

L86 ANSWER 13 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

AN 86106802 EMBASE

DN 1986106802

TI Reduced incretin effect in Type 2 (non-insulin-dependent) diabetes.

AU **Nauck** M.; Stockmann F.; Ebert R.; Creutzfeldt W.

CS Department of Medicine, Division of Gastroenterology and Metabolism, D-3400 Gottingen, Germany

SO Diabetologia, (1986) 29/1 (46-52).
CODEN: DBTGAJ

CY Germany

DT Journal

FS 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry

LA English

AB Integrated incremental immunoreactive insulin and connecting peptide responses to an oral **glucose** load of 50 g and an 'isoglycaemic' intravenous **glucose infusion**, respectively, were measured in 14 Type 2 (non-insulin-dependent) diabetic patients and 8 age- and weight-matched metabolically healthy control subjects. Differences between responses to oral and intravenous **glucose** administration are attributed to factors other than **glucose** itself (incretin effect). Despite higher **glucose** increases, immunoreactive insulin and connecting peptide responses after oral **glucose** were delayed in diabetic patients. Integrated responses were not significantly different between both groups. However, during 'isoglycaemic' intravenous **infusion**, insulin and connecting peptide responses were greater in diabetic patients than in control subjects as a consequence of the higher glycaemic stimulus. The contribution of incretin factors to total insulin responses was 72.8 .+-. 6.9% (100% = response to oral load) in control subjects and 36.0 .+-. 8.8% in diabetic patients (p .ltoreq. 0.05). The contribution to connecting peptide responses was 58.4 .+-. 7.6% in control subjects and 7.6 .+-. 14.5% (p .ltoreq. 0.05) in diabetic patients. Ratios of integrated insulin to connecting peptide responses suggest a reduced (hepatic) insulin extraction in control subjects after oral as compared to intravenous **glucose**. This was not the case in diabetic patients. Immunoreactive **gastric inhibitory polypeptide** responses were not different between control subjects and diabetic patients. A reduced or lost incretin effect in the face of normal **gastric inhibitory polypeptide** response in Type 2 diabetic patients may be explained by decreased sensitivity of the B cells towards the insulinotropic effect of **gastric inhibitory polypeptide** or to hyposecretion or reduced

effectiveness of as yet unidentified humoral or nervous gut factors with incretin activity.

CT Medical Descriptors:
*incretin effect
*non insulin dependent diabetes mellitus
insulin release
endocrine system
priority journal
etiology
biological model
human
adult
Drug Descriptors:
***gastric inhibitory polypeptide**
RN (**gastric inhibitory polypeptide**)
59392-49-3

L86 ANSWER 14 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 86027574 EMBASE
DN 1986027574
TI Effects of **gastric inhibitory polypeptide** in the response to **prolonged parenteral** or enteral alimentation in rats.
AU Baer A.R.; Dupre J.
CS Department of Medicine, University of Western Ontario, London, Ont. N6A 5A5, Canada
SO Diabetes, (1985) 34/11 (1108-1112).
CODEN: DIAEAZ
CY United States
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
048 Gastroenterology
030 Pharmacology
LA English
AB To examine the effects of long-term elevation of plasma **gastric inhibitory polypeptide** (**GIP**), the responses to **parenteral** (PA) or enteral (EA) alimentation were studied in conscious rats with duodenal and venous cannulae. A weight-maintaining liquid diet (84% as **glucose**, 16% as amino acids) was infused at a constant rate for 6 days by either route, and daily blood samples were taken. A subset of animals receiving PA also received porcine **GIP** with the infusate (PA plus **GIP**; plateau plasma immunoreactive **GIP**, IRGIP, 610 .+-. 120 pg/ml). With PA, plasma IRGIP did not change from basal levels, whereas with EA IRGIP rose to virtual plateau levels (mean 530 .+-. 110 pg/ml). In the steady state, plasma immunoreactive insulin (IRI) was significantly lower with EA (mean, 153 .+-. 5 .mu.U/ml) than with PA (mean, 226 .+-. 15 .mu.U/ml), which in turn was lower than with PA plus **GIP** (mean, 375 .+-. 23 .mu.U/ml, P < 0.001 by ANOVA). A similar ranking of plasma **glucose** levels occurred in the steady state, with means of 113 .+-. 7 (EA), 126 .+-. 3 (PA), and 184 .+-. 9 (PA plus **GIP**) mg/dl (P < 0.001 by ANOVA). To assess the response to transient hyperglycemia in the steady state, an intravenous **glucose** bolus was given to each group on the fifth day. Peak plasma IRI levels did not differ among the three groups; however, the **glucose** disappearance rate was significantly slower with PA plus **GIP** compared with either EA or PA. Assuming that porcine **GIP** did not stimulate **glucose** production, this peptide appeared to induce hyperinsulinemia with insulin resistar **parenteral** alimentation. The contrasting features of relatively low **glucose** and insulin levels during enteral alimentation associated with high levels of endogenous IRGIP in the blood sugg either (1) that the findings depend on variations of **GIP** or its actions in the different species, or (2) that mechanisms originat the intestine act to preserve insulin sensitivity during absorpti nutrients from the gut under physiologic conditions.

CT Medical Descriptors:
*alimentation
*drug blood level
*drug mechanism
*drug monitoring
*food drug interaction
*insulin resistance
*insulin sensitivity
*intestine absorption
hyperglycemia
hyperinsulinemia
plasma
rat
endocrine system
priority journal
intravenous drug administration
oral drug administration
preliminary communication
nonhuman
small intestine
animal experiment
Drug Descriptors:
***gastric inhibitory polypeptide**
***glucose**
*insulin
RN (**gastric inhibitory polypeptide**)
59392-49-3; (**glucose**) **50-99-7**, 84778-64-3;
(insulin) 9004-10-8

=> fil medline

FILE 'MEDLINE' ENTERED AT 14:01:50 ON 10 APR 2000

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=> d his l88-

(FILE 'EMBASE' ENTERED AT 13:32:58 ON 10 APR 2000)

FILE 'EMBASE' ENTERED AT 13:43:41 ON 10 APR 2000

FILE 'MEDLINE' ENTERED AT 13:44:01 ON 10 APR 2000
L88 208876 S L46
L89 2502 S L75
L90 1230 S L88 AND L89
L91 880 S L90 AND PY<=1995
L92 44 S L91 AND ?PARENTERAL?
L93 23193 S (GLUCOSE (L) (AD OR PD OR TH OR PK))/CT
L94 28 S L92 AND L93
L95 294 S ((GASTRIC INHIBITORY POLYPEPTIDE)(L)(PD OR PK OR AD OR TU))/C
L96 5 S L95 AND L94
L97 7 S L94 AND GLUCAGON?

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L98          15 S L92 AND GLUCAGON?
L99           8 S L98 NOT L97
L100       7689 S (GLUCAGON (L) (PD OR PK OR TU OR AD))/CT
L101          1 S L100 AND L94
L102          6 S L96,L101

     FILE 'MEDLINE' ENTERED AT 14:01:50 ON 10 APR 2000

=> d all tot


L102 ANSWER 1 OF 6  MEDLINE
AN   86194059     MEDLINE
DN   86194059
TI   Effect of GIP on insulin release to intravenous glucose
     infusion in hyperthyroid rats.
AU   Muller M K; Hellwig J; Schafer A; Goebell H; Brown J C
SO   HORMONE AND METABOLIC RESEARCH, (1986 Mar) 18 (3) 163-6.
     Journal code: GBD. ISSN: 0018-5043.
CY   GERMANY, WEST: Germany, Federal Republic of
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   198608
AB   Triiodothyronine induced hyperthyroidism caused significantly elevated
     basal and stimulated glucose and insulin levels in rats. The
     release of Gastric Inhibitory Polypeptide (
     GIP) following an oral glucose load was not
     significantly different between euthyroid and hyperthyroid rats. The
     insulin response, however, was significantly higher in hyperthyroid rats.
     Following intravenous glucose hyperthyroid rats showed a
     diminished insulin response when compared with euthyroid rats but
     intravenous infusion of glucose together with GIP
     caused a significantly higher insulin response in hyperthyroid rats. It is
     hypothesized that in hyperthyroidism there is an increased sensitivity to
     the insulinotropic action of GIP and that this mechanism could
     emphasize the importance of the enteroinsular axis in pathophysiological
     states.
CT   Check Tags: Animal; Male; Support, Non-U.S. Gov't
      Administration, Oral
      Blood Glucose: ME, metabolism
      Disease Models, Animal
     *Gastric Inhibitory Polypeptide: PD, pharmacology
      Glucose: AD, administration & dosage
     *Glucose: PD, pharmacology
      Hyperthyroidism: CI, chemically induced
     *Hyperthyroidism: PP, physiopathology
      Infusions, Parenteral
      Insulin: BL, blood
     *Insulin: SE, secretion
      Rats
      Rats, Inbred Strains
      Triiodothyronine
RN   11061-68-0 (Insulin); 50-99-7 (Glucose); 59392-49-3
     (Gastric Inhibitory Polypeptide); 6893-02-3 (Triiodothyronine)
CN   0 (Blood Glucose)

L102 ANSWER 2 OF 6  MEDLINE
AN   86151365     MEDLINE
DN   86151365
TI   The priming effect of glucose on the gastric
     inhibitory polypeptide-induced insulin release.
AU   Jorde R; Amland P F; Burhol P G
SO   SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY, (1986 Jan) 21 (1)
     47-50.
     Journal code: UCS. ISSN: 0036-5521.
```

CY Norway
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198606
AB Six healthy subjects were given a 15-min intravenous infusion of **gastric inhibitory polypeptide** (**GIP**) in a dose of 1.0 microgram X kg-1 X h-1 at a mean blood **glucose** level of 4.9 mmol/l after a priming infusion with **glucose**. A significant insulin release was seen during the **GIP** infusion, an effect that could not be demonstrated without the priming **glucose** infusion.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Blood Glucose: AN, analysis
Gastric Inhibitory Polypeptide: BL, blood
***Gastric Inhibitory Polypeptide: PD, pharmacology**
Glucose: AD, administration & dosage
***Glucose: PD, pharmacology**
Infusions, Parenteral
Insulin: BL, blood
*Insulin: SE, secretion
Time Factors
RN 11061-68-0 (Insulin); **50-99-7 (Glucose)**; **59392-49-3 (Gastric Inhibitory Polypeptide)**
CN 0 (Blood **Glucose**)

L102 ANSWER 3 OF 6 MEDLINE
AN 86008905 MEDLINE
DN 86008905
TI Effects of atropine and **gastric inhibitory polypeptide** on hepatic **glucose** uptake and insulin extraction in conscious dogs.
AU Chap Z; Ishida T; Chou J; Lewis R; Hartley C; Entman M; Field J B
NC AM 25253 (NIADDK)
AM 27685 (NIADDK)
SO JOURNAL OF CLINICAL INVESTIGATION, **(1985 Sep)** 76 (3) 1174-81.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198601
AB Previous studies comparing the effects of oral, intraportal, and peripheral venous administration of **glucose** in conscious dogs demonstrated a significant increase in hepatic extraction of insulin only after oral **glucose**, but similar hepatic uptake of **glucose** after oral and intraportal **glucose**, which was greater than that after peripheral intravenous **glucose** infusion. This study evaluated the effect of atropine blockade of the parasympathetic nervous system on the increased fractional hepatic extraction of insulin and the role of **gastric inhibitory polypeptide** (**GIP**) on augmented hepatic uptake of oral **glucose** in conscious dogs with chronically implanted Doppler flow probes on the portal vein and hepatic artery, and catheters in the portal and hepatic veins and carotid artery. Since atropine infusion decreased absorption of **glucose**, and in order to achieve comparable portal vein levels of **glucose** and insulin, the dogs receiving atropine were given 1.9 +/- 0.1 g/kg **glucose**, compared with the control dogs who received 1.1 +/- 0.1 g/kg. The percentage of the **glucose** load that was absorbed was greater in the dogs not given atropine (80 +/- 4 vs. 44 +/- 7%), but because of the different loads, the absolute amount of **glucose** absorbed was similar in both groups (20.2 +/- 1.6 vs. 21.7 +/- 4.1 g). Although delayed by atropine, the peak portal vein **glucose** and insulin concentrations and the amounts presented to the liver were similar in both groups. However, the increased portal vein

plasma flow and fractional hepatic extraction of insulin observed after oral **glucose** was not observed in the dogs infused with atropine. The net hepatic **glucose** uptake after oral **glucose** was significantly less at 10, 20, and 45 min in the atropine-treated dogs, and the area under the curve over the 180-min period was 44% less. However, the latter was not statistically significant. Infusion of **GIP** with peripheral intravenous **glucose** did not increase hepatic uptake of **glucose** or the fractional hepatic extraction of insulin compared with peripheral intravenous **glucose** alone. These results indicate an important role for parasympathetic innervation in the augmented fractional hepatic extraction of insulin, and increased portal vein plasma flow after oral **glucose**. Although a relationship between the augmented fractional extraction of insulin and the net hepatic **glucose** uptake may exist, it does not necessarily indicate that the former is required for the latter. Such parasympathetic innervation may be involved in the greater removal of **glucose** by the liver after oral compared with peripheral **glucose** administration.(ABSTRACT TRUNCATED AT 400 WORDS)

CT Check Tags: Animal; Female; Male; Support, U.S. Gov't, P.H.S.
Administration, Oral
Atropine: AD, administration & dosage
*Atropine: PD, pharmacology
Blood Glucose: ME, metabolism
Dogs
Gastric Inhibitory Polypeptide: AD, administration & dosage
***Gastric Inhibitory Polypeptide: PD, pharmacology**
Glucose: AD, administration & dosage
***Glucose: ME, metabolism**
Hepatic Artery
Hepatic Veins
Infusions, Parenteral
*Insulin: BL, blood
*Liver: ME, metabolism
Portal Vein

RN 11061-68-0 (Insulin); **50-99-7 (Glucose)**; 51-55-8 (Atropine); **59392-49-3 (Gastric Inhibitory Polypeptide)**

CN 0 (Blood **Glucose**)

L102 ANSWER 4 OF 6 MEDLINE

AN 85218446 MEDLINE

DN 85218446

TI Effect of intravenously infused porcine **GIP** on serum insulin in obese and lean subjects studied with the hyperglycemic clamp technique.

AU Amland P F; Jorde R; Burhol P G; Giercksky K E

SO SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY, **(1985 Apr)** 20 (3) 309-14.
Journal code: UCS. ISSN: 0036-5521.

CY Norway

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198509

AB To ascertain whether an altered sensitivity to **gastric inhibitory polypeptide** (**GIP**) in morbidly obese subjects can play a role in the postprandial hyperinsulinemia seen in this condition, eight obese and eight control subjects were studied with an intravenous infusion of porcine **GIP**. The blood **glucose** was maintained at 4 mmol/l above the basal level by a hyperglycemic clamp technique. Although the mean serum insulin level was higher in the obese group throughout the study, the shapes of the serum insulin curves were almost identical in the two groups after the **GIP** infusion. This together with the normal **GIP** secretion found in obese subjects question the existence of a causal relationship between an overactive entero-insular axis and the hyperinsulinemia found in these subjects.

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't

Adult
Blood Glucose: AN, analysis
Body Weight
***Gastric Inhibitory Polypeptide: AD, administration & dosage**
Gastric Inhibitory Polypeptide: BL, blood
*Gastrointestinal Hormones: AD, administration & dosage
Glucose: AD, administration & dosage
Infusions, Parenteral
*Insulin: BL, blood
Insulin: SE, secretion
Middle Age
*Obesity: BL, blood
Secretory Rate: DE, drug effects
RN 11061-68-0 (Insulin); **50-99-7 (Glucose); 59392-49-3 (Gastric Inhibitory Polypeptide)**
CN 0 (Blood **Glucose**); 0 (Gastrointestinal Hormones)

L102 ANSWER 5 OF 6 MEDLINE
AN 83288121 MEDLINE
DN 83288121
TI Preservation of incretin activity after removal of **gastric inhibitory polypeptide** (**GIP**) from rat gut extracts by immunoadsorption.
AU Ebert R; Unger H; Creutzfeldt W
SO DIABETOLOGIA, **(1983 Jun)** 24 (6) 449-54.
Journal code: E93. ISSN: 0012-186X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198312
AB The action of watery rat gut extracts on **glucose**-induced insulin release in anaesthetized rats was examined before and after removal of **GIP** by immunoadsorption. Infusions of **GIP**-containing rat gut extracts nearly doubled the insulin release induced by intravenous **glucose** (1 g X kg -1 X h -1). Peak insulin secretion was 98 +/- 11 mU/l (mean +/- SEM) after intravenous **glucose** and increased to 178 +/- 16 mU/l following infusion of **glucose** plus gut extract (p less than 0.005). After injection of **GIP** antiserum in sufficient amounts to neutralize the **GIP** activity in the gut extract preparation, the additional insulin release due to the gut extract was reduced by only 30%. After complete removal of **GIP** from gut extracts by immuno-absorption, more than 50% of the incretin effect remained. These data suggest that the insulinotropic activity of rat gut extracts can only be partially related to **GIP**. The existence of additional insulinotropic gut factors which may also be released following oral **glucose** is postulated.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Antibodies: AD, administration & dosage
***Gastric Inhibitory Polypeptide: AD, administration & dosage**
Gastric Inhibitory Polypeptide: IM, immunology
*Gastrointestinal Hormones: AD, administration & dosage
Glucose: AD, administration & dosage
Glucose: ME, metabolism
Immunosorbent Techniques
Infusions, Parenteral
*Insulin: SE, secretion
*Intestines: ME, metabolism
*Peptide Fragments: ME, metabolism
Rats
Rats, Inbred Strains
Time Factors
*Tissue Extracts: AD, administration & dosage
Tissue Extracts: AN, analysis
RN 11061-68-0 (Insulin); **119637-73-9 (glucagon-like peptide I (7-36)amide); 50-99-7 (Glucose); 59392-49-3 (Gastric**

Inhibitory Polypeptide)
CN 0 (Antibodies); 0 (Gastrointestinal Hormones); 0 (Peptide Fragments); 0 (Peptides); 0 (Tissue Extracts)

L102 ANSWER 6 OF 6 MEDLINE
AN 77259542 MEDLINE
DN 77259542
TI Augmented **gastric inhibitory polypeptide** response to intraduodenal **glucose** by exogenous gastrin and cholecystokinin.
AU Sirinek K R; Cataland S; O'Dorisio T M; Mazzaferri E L; Crockett S E; Pace W G
SO SURGERY, **(1977 Oct)** 82 (4) 438-42.
Journal code: VC3. ISSN: 0039-6060.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 197712
CT Check Tags: Animal
*Cholecystokinin: PD, pharmacology
Dogs
Duodenum
Fasting
***Gastric Inhibitory Polypeptide: ME, metabolism**
*Gastrins: PD, pharmacology
*Gastrointestinal Hormones: ME, metabolism
Glucagon: PD, pharmacology
***Glucose: AD, administration & dosage**
Glucose: DU, diagnostic use
Glucose: PD, pharmacology
Infusions, Parenteral
Pentagastrin: PD, pharmacology
Secretin: PD, pharmacology
Sodium Chloride: PD, pharmacology
Stimulation, Chemical

=> fil wpids

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                E NAUCK M/AU
L103            5 S E3,E4
                E WAGNER F/AU
L104          139 S E3,E4
L105          144 S L103,L104
                E GLUCOSE/DCN
                E E3+ALL/DCN
L106         7698 S E2 OR 0038/DRN
                E GLUCOSE/DCN
                E E8+ALL/DCN
L107           18 S E2
                E GLUCOSE/DCN
                E E9+ALL/DCN
L108        30290 SEA "L814"/M0,M1,M2,M3,M4,M5,M6
L109        45926 S L106-L108 OR GLUCOSE
L110           97 S L109 AND (GLUCAGON? OR GLUCACON?)
L111           32 S L109 AND (GLP OR GIP)
L112           11 S L109 AND GASTRI? () INHIBIT? () (PEPTIDE OR POLYPEPTIDE OR PO
L113          104 S L110-L112
L114           27 S L109 AND A61K038-26/IC,ICM,ICS,ICA,ICI
L115          110 S L113,L114
L116            7 S L109 AND L105
L117            1 S L116 AND PARENTER?
L118           15 S L110-L115 AND ?PARENTERAL?
L119            1 S L118 AND L105
L120            2 S D03-H01T?/MC AND L110-L115
L121            2 SEA (L110 OR L111 OR L112 OR L113 OR L114 OR L115) AND
                R023/M0,M1,M2,M3,M4,M5,M6
L122            5 S L110-L115 AND A61K009-08/IC,ICM,ICS,ICA,ICI
L123           19 S L118-L122
L124           13 SEA M782/M0,M1,M2,M3,M4,M5,M6 AND L123
L125            6 S L123 NOT L124
L126            5 S L124 AND (NUTRITION OR TREAT?)/TI
L127            2 S L126 NOT (TRANSDERMAL OR SHOCK OR AMYLIN)/TI

     FILE 'WPIDS' ENTERED AT 14:18:37 ON 10 APR 2000

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L127 ANSWER 1 OF 2  WPIDS COPYRIGHT 2000   DERWENT INFORMATION LTD
AN   1997-146440 [14]   WPIDS
DNC  C1997-046880
TI   Compsns. for parenteral nutrition - contg.
     glucagon-like peptide 1 and/or gastric
     inhibitory peptide.
DC   B04 D13
IN   NAUCK, M; NAUCK, M A; WAGNER, F W
PA   (BION-N) BIONEBRASKA INC; (NAUC-I) NAUCK M A; (NAUK-I) NAUCK M A; (NAUC-I)
     NAUCK M
CYC  73
PI   DE 19530865    A1 19970227 (199714)*       3p    A23L001-29
     WO 9707814     A1 19970306 (199716)  EN   20p    A61K038-26      <--
        RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD
            SE SZ UG
         W: AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU
            IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ
            PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
     AU 9669006     A  19970319 (199728)             A61K038-26      <--
     EP 851763      A1 19980708 (199831)  EN         A61K038-26      <--
         R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
     CZ 9800508     A3 19990113 (199908)             A61K038-26      <--
     CN 1195992     A  19981014 (199909)             A61K038-26      <--
     JP 11514972    W  19991221 (200010)       22p   A61K038-00
ADT  DE 19530865 A1 DE 1995-19530865 19950822; WO 9707814 A1 WO 1996-US13615
     19960822; AU 9669006 A AU 1996-69006 19960822; EP 851763 A1 EP 1996-929722
```

19960822, WO 1996-US13615 19960822; CZ 9800508 A3 WO 1996-US13615 19960822, CZ 1998-508 19960822; CN 1195992 A CN 1996-196938 19960822; JP 11514972 W WO 1996-US13615 19960822, JP 1997-510445 19960822

FDT AU 9669006 A Based on WO 9707814; EP 851763 A1 Based on WO 9707814; CZ 9800508 A3 Based on WO 9707814; JP 11514972 W Based on WO 9707814

PRAI DE 1995-19530865 19950822

IC ICM A23L001-29; A61K038-00; **A61K038-26**
ICS A23L001-305; **A61K009-08**; A61K009-22; A61K031-00; A61K031-70; A61K038-22

AB DE 19530865 A UPAB: 19970407
Compsns. for **parenteral** nutrition contain **glucagon**-like peptide 1 [7-36 amide] and/or **gastric inhibitory peptide**.
ADVANTAGE - High-calorie nutrition can be given with reduced risk of hyperglycaemia and with reduced risk of hypoglycaemia compared with the use of insulin.
Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-N02; B14-E11; **D03-H01T2**

L127 ANSWER 2 OF 2 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1996-010691 [01] WPIDS

DNC C1996-003346

TI **Treating** insulin-requiring diabetes with **glucagon**-like peptide or derivs. - opt. together with insulin, provides improved control of blood **glucose** levels.

DC B04

IN DUPRE, J

PA (AMYL-N) AMYLIN PHARM INC; (LONH-N) LONDON HEALTH ASSOC; (AMYL) AMYLIN PHARM INC

CYC 65

PI WO 9531214 A1 19951123 (199601)* EN 29p A61K038-26 <--
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN
AU 9524044 A 19951205 (199620) A61K038-26 <--
EP 762890 A1 19970319 (199716) EN A61K038-26 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 10500114 W 19980106 (199811) 28p A61K038-26 <--
AU 711611 B 19991014 (200001) A61K038-26 <--

ADT WO 9531214 A1 WO 1995-CA287 19950512; AU 9524044 A AU 1995-24044 19950512; EP 762890 A1 EP 1995-917874 19950512, WO 1995-CA287 19950512; JP 10500114 W JP 1995-529262 19950512, WO 1995-CA287 19950512; AU 711611 B AU 1995-24044 19950512

FDT AU 9524044 A Based on WO 9531214; EP 762890 A1 Based on WO 9531214; JP 10500114 W Based on WO 9531214; AU 711611 B Previous Publ. AU 9524044, Based on WO 9531214

PRAI GB 1994-9496 19940512

REP 2.Jnl.Ref; WO 9111457; WO 9325579

IC ICM **A61K038-26**
ICS A61K038-28

ICI **A61K038-26**, A61K038:

AB WO 9531214 A UPAB: 19971021
Insulin-requiring diabetes is treated by admin of (a) insulin and (b) **glucagon**-like peptide 1 (7-37) (IIa), **glucagon**-like peptide 1 (7-36) amide (IIb), or an analogue or fragment of (IIa) or (IIb). Also new is the treatment of type I diabetes with these peptides alone without using insulin.
USE - The method is used in human medicine for the treatment of types I or II diabetes. The use of (IIa)/(IIb) alone may be suitable for treating some cases of type I, partic. in remission phase subjects. The peptides may be given orally, nasally or **parenterally**.
ADVANTAGE - The use of (IIa)/(IIb), opt. in (synergistic) combination with oral hypoglycaemics, is already known for treatment of non-insulin

dependent diabetes. It is now found, that these peptides improve control of glycaemia in patients requiring insulin. When administered before a meal, they delay the increase in blood **glucose** levels by inhibiting emptying of the stomach (insulin secretion is not affected) and thus, should be effective even in patients with no residual insulin-secreting capacity. The use of the peptides may make it possible to reduce the overall insulin dose.
Dwg.1/6
FS CPI
FA AB; GI
MC CPI: B04-J03A; B04-N04; B14-S04

=> fil hcaplus

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FILE LAST UPDATED: 9 Apr 2000 (20000409/ED)

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L1 3 S 58367-01-4 OR 921-60-8 OR 50-99-7
L2 1 S 59392-49-3
L3 1 S 89750-14-1

FILE 'HCAPLUS' ENTERED AT 14:31:44 ON 10 APR 2000
L4 106038 S L1
L5 1427 S L2 OR L3
L6 250112 S L4 OR GLUCOSE
L7 20351 S L5 OR GLUCAGON? OR GLUCACON? OR GIP OR GLP OR GASTRIC INHIBIT
L8 8020 S L6 AND L7
L9 86 S L8 AND ?PARENTERAL?
L10 81 S L2 (L) THU/RL OR L3 (L) THU/RL
L11 45 S L10 AND L8
L12 6789 S L8 AND PY<=1995
L13 42 S L8 AND PRY<=1995
L14 40 S L8 AND PRY.B<=1995
L15 50 S L8 AND AY<=1995
L16 45 S L8 AND AY.B<=1995

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L17        6798 S L12-L16
L18           4 S L17 AND L10
L19          75 S L17 AND L9
L20           1 S L19 AND L18
L21           1 S 63/SC,SX AND L17 AND L9
L22           5 S 1/SC,SX AND L17 AND L9
L23           1 S 17/SC,SX AND L17 AND L9
L24          50 S 18/SC,SX AND L17 AND L9
L25          31 S NUTRI?/CW AND L17 AND L9
L26           7 S L20-L23
L27          52 S L24-L26 NOT (NAUCK M? OR WAGNER F?)/AU
L28           9 S COMPOSITION AND L27
L29        2053 S L1 (L) THU/RL OR L1 (L) FFD/RL
L30          81 S L2 (L) FFD/RL OR L3 (L) FFD/RL OR L2 (L) THU/RL OR L3 (L) THU
L31           2 S L29 AND L30
L32           0 S L27 AND L29
L33           0 S L27 AND L30
L34           1 S L31 NOT NAUCK ?/AU

     FILE 'HCAPLUS' ENTERED AT 14:42:10 ON 10 APR 2000

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L34  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2000 ACS
AN   1999:626062  HCAPLUS
DN   131:262604
TI   Pharmaceutical compositions for prolonged peptide release and preparation
     method
IN   Pellet, Marc; Bismuth, Frederic
PA   Societe de Conseils de Recherches et d'Applications Scientifiques
     (S.C.R.A.S, Fr.
SO   PCT Int. Appl., 23 pp.
     CODEN: PIXXD2
DT   Patent
LA   French
IC   ICM  A61K038-09
     ICS  A61K038-31; A61K009-14; A61K047-26
CC   63-6 (Pharmaceuticals)
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
PI   WO 9948517         A1   19990930       WO 1999-FR667     19990322
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     FR 2776520         A1   19991001       FR 1998-3667      19980325
     AU 9929384         A1   19991018       AU 1999-29384     19990322
PRAI FR 1998-3667      19980325
     WO 1999-FR667     19990322
AB   Novel solid or semi-solid pharmaceutical compns. comprising a sol. peptide
     salt capable of jellifying, having a high sp. surface area is disclosed.
     Said compns. can also comprise an excipient and/or water.  Once injected
     to a patient, the compns. jellify and release the peptide salt for a long
     time interval not less than 15 days.  Lanreotide acetate (I) with sp.
     surface of 0.61 m2/g was dissolved in water at 30 g/L.  The soln. was then
     lyophilized to obtain I with sp. surface of 5.41 m2/g.  A homogeneous
     soln. of 3 g I in 6.927 mL water was prepd. for direct injection to a
     patient.
ST   prolonged release pharmaceutical injection peptide; lanreotide prolonged
```

release pharmaceutical injection
IT Drug delivery systems
(injections, sustained release; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Solvents
(org.; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Surfactants
(pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Blood-coagulation factors
Bone morphogenetic proteins
Carbohydrates, biological studies
Enkephalins
Interleukin 2
Interleukins
Peptides, biological studies
Platelet-derived growth factors
Polysaccharides, biological studies
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyhydric; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Thymus hormones
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thymostimulin; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Integrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.IIb.beta.3; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT 116243-73-3, Endothelin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; pharmaceutical compns. for prolonged peptide release and prepn. method)
IT 50-56-6, Oxytocin, biological studies 50-70-4, Sorbitol, biological studies **50-99-7**, Glucose, biological studies 58-82-2, Bradykinin 63-42-3, Lactose 69-65-8, Mannitol 1066-17-7, Colistin 1393-25-5, Secretin 1404-26-8, Polymyxin B 1405-87-4, Bacitracin 1405-97-6, Gramicidin 1407-47-2, Angiotensin 9001-01-8, Kallikrein 9002-60-2, Acth, biological studies 9002-61-3, Human chorionic gonadotropin 9002-62-4, Prolactin, biological studies 9002-64-6, Parathyroid hormone 9002-67-9, Luteinizing hormone 9002-68-0, Follicle-stimulating hormone 9002-71-5, Thyroid stimulating hormone 9002-72-6, Growth hormone 9002-76-0, Gastrin 9002-79-3, Melanocyte stimulating hormone 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 9011-97-6, Cholecystokinin 9015-68-3, Asparaginase 9034-39-3, Somatoliberin 9034-40-6, Lh rh 9035-54-5 9039-53-6, Urokinase 9061-61-4, Nerve growth factor 9063-57-4, Tuftsin 9066-59-5, Lysozyme hydrochloride 11000-17-2, Vasopressin 11096-26-7,

Erythropoietin 17650-98-5, Caerulein 24305-27-9, Thyrotropin releasing hormone 31362-50-2, Bombesin 33507-63-0, Substance P 37221-79-7, Vasoactive Intestinal peptide 39379-15-2, Neurotensin 51110-01-1, Somatostatin 51110-01-1D, Somatostatin, analogs and derivs. 52906-92-0, Motilin 53714-56-0, Leuprorelin 57773-63-4, Triptoreline 57982-77-1, Buserelin **59392-49-3**, Gastric inhibitory polypeptide 60118-07-2, Endorphin 60529-76-2, Thymopoietin 61512-21-8, Thymosin 62229-50-9, Epidermal growth factor 62683-29-8, Colony stimulating factor 63340-72-7, Thymus humoral factor 65807-02-5, Goserelin 70904-56-2, Kyotorphin 74913-18-1, Dynorphin 78922-62-0, Serum thymic factor 79517-01-4, Octreotide acetate 80043-53-4, Gastrin releasing peptide 82785-45-3, Neuropeptide y 83150-76-9, Octreotide 83652-28-2, Calcitonin gene related peptide 103370-86-1, Parathyroid hormone related peptide 106388-42-5, Peptide yy 108736-35-2, Lanreotide 127984-74-1, Lanreotide acetate 137061-48-4, Pacap 160296-12-8 164003-54-7, TFX-Thymomodulin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for prolonged peptide release and prepn. method)